



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 112711

TO: Dwayne C Jones  
Location: ~~CM4-2D01~~ Rem E4A71  
Art Unit: 1614  
Monday, February 02, 2004

Case Serial Number: 09/700142

From: Barb O'Bryen  
Location: Biotech-Chem Library  
Remsen E01A69  
Phone: 571-272-2518

barbara.obryen@uspto.gov

### Search Notes

Note: Examiner moves to Remsen 2-4-04  
Rem E4A71

WO 97/07833  
2 of 55  
11 of 55 (163)  
~~6,648,213~~ differ entry  
~~6,598,278~~ "  
~~6,118,231~~ "  
~~6,126,756~~ "  
5,934,323  
4-5,658,582

=> fil reg; d ide

FILE 'REGISTRY' ENTERED AT 16:05:43 ON 02 FEB 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 FEB 2004 HIGHEST RN 644944-93-4

DICTIONARY FILE UPDATES: 1 FEB 2004 HIGHEST RN 644944-93-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 9004-61-9/ REGISTRY

CN **Hyaluronic acid (8CI, 9CI)** (CA INDEX NAME)

OTHER NAMES:

CN ACP

CN ACP (polysaccharide)

CN ACP gel

CN Durolane

CN Genzyme 9983

CN HA 9

CN Hy 20

CN Hyalofill

CN Hyaluronan

CN Hylan G-F 20

CN Hylartil

CN Luronit

CN Mucoitin

CN Sepracoat

CN Sofast

CN Synvisc

DR 165324-65-2, 9039-38-7, 37243-73-5, 29382-75-0

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyester, Polyester formed

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

10636 REFERENCES IN FILE CA (1907 TO DATE)

791 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

## 10656 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=&gt; d ide 130

L30 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 100-51-6/REGISTRY  
CN Benzenemethanol (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN **Benzyl alcohol (8CI)**  
OTHER NAMES:  
CN (Hydroxymethyl)benzene  
CN .alpha.-Hydroxytoluene  
CN .alpha.-Toluenol  
CN Benzenecarbinol  
CN Benzylic alcohol  
CN NSC 8044  
CN Phenylcarbinol  
CN Phenylmethanol  
CN Phenylmethyl alcohol  
CN Summorl BK 20  
FS 3D CONCORD  
DR 1336-27-2, 185532-71-2  
MF C7 H8 O  
CI COM  
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM\*, DIOGENES, DIPPR\*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPAT, ENCOMPAT2, GMELIN\*, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM\*, PIRA, PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VTB  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

HO-CH<sub>2</sub>-Ph

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

19967 REFERENCES IN FILE CA (1907 TO DATE)  
406 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
20021 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=&gt; d que 132

L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31

*hyaluronic acid +  
benzyl alcohol as components  
in same record*

=> fil capl

FILE 'CAPLUS' ENTERED AT 17:10:50 ON 02 FEB 2004

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FILE COVERS 1907 - 2 Feb 2004 VOL 140 ISS 6

FILE LAST UPDATED: 1 Feb 2004 (20040201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

*Inventors*

=> d que 13

L1 19 SEA FILE=CAPLUS ABB=ON PAVESIO A?/AU  
L2 152 SEA FILE=CAPLUS ABB=ON CALLEGARO L?/AU  
L3 6 SEA FILE=CAPLUS ABB=ON L1 AND L2

=> d ibib ab 13 1-6

L3 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:695832 CAPLUS

DOCUMENT NUMBER: 137:222118

TITLE: Grafts for the repair of osteochondral defects

INVENTOR(S): **Pavesio, Alessandra; Callegaro, Landranco**

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Italy

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070030	A1	20020912	WO 2002-EP1224	20020206
WO 2002070030	C1	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG  
EP 1357953 A1 20031105 EP 2002-726105 20020206

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

## PRIORITY APPLN. INFO.:

IT 2001-PD32 A 20010209  
WO 2002-EP1224 W 20020206

AB The invention concerns the prepn. and use of a biocompatible, biocomponent material constituted by: (a) a three-dimensional matrix of hyaluronic acid derivs. with a structure contg. empty spaces; (b) a porous, three-dimensional matrix constituted by a ceramic material; (c) possibly contg. pharmacol. or biol. active ingredients. Cultured mesenchymal stem cells exposed to .beta.1-transforming growth factors were loaded into a sponge made of a hyaluronan deriv. (Hyaff-11) for the construction of the cartilage component of the composite graft. Mesenchymal stem cells exposed to osteogenic supplement were loaded into a porous calcium phosphate ceramic component for bone formation. Cell-loaded Hyaff-11 sponge and ceramic were assembled and joined together with fibrin glue to form a composite osteochondral graft. Said graft was incubated at 37.degree. for 30 min and then grafted s.c. into the backs of syngeneic rats and the animals were sacrificed 6 wk later. After six weeks, well-organized fibrocartilage was distributed through the material that is partially absorbed. The sep. formation of cartilage and bone could be seen in the two material. Neither the bone tissue nor the cartilage crosses the tidemark between the two materials. At the same time, the two materials formed a structurally integrated composite material thanks to the presence of fibrous tissue and collagen fibers that do cross tidemark.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:624504 CAPLUS

DOCUMENT NUMBER: 137:129932

TITLE: Injectable biocompatible and biodegradable compositions containing a hyaluronic acid derivative and chondrogenic cells for treatment of cartilaginous defects

INVENTOR(S): Radice, Marco; Pastorello, Andrea; Pavesio, Alessandra; Callegaro, Lanfranco

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Italy

SOURCE: Ital., 17 pp.  
CODEN: ITXXBY

DOCUMENT TYPE: Patent

LANGUAGE: Italian

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IT 1302534	B1	20000905	IT 1998-PD298	19981221
WO 2000037124	A1	20000629	WO 1999-IB2077	19991221
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

JP 2002532568 T2 20021002 JP 2000-589234 19991221

US 2002076810 A1 20020620 US 2001-887757 20010621

## PRIORITY APPLN. INFO.:

IT 1998-PD298 A 19981221

WO 1999-IB2077 W 19991221

AB Injectable compns. are disclosed which are biocompatible and biodegradable and comprise at least one hyaluronic acid deriv. as well as chondrogenic cells plus pharmacol. active substances for repair of articular cartilage defects.

L3 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:300558 CAPLUS

DOCUMENT NUMBER: 134:300839

TITLE: Formulations of hyaluronic acid for delivery of osteogenic proteins

INVENTOR(S): Kim, Hyun; Li, Rebecca; **Pavesio, Alessandra;**  
**Callegaro, Lanfranco**

PATENT ASSIGNEE(S): Genetics Institute, Inc., USA; Fidia Advanced Biology

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028602	A1	20010426	WO 2000-US28468	20001013
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1223990	A1	20020724	EP 2000-970914	20001013
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
JP 2003512341	T2	20030402	JP 2001-531430	20001013
PRIORITY APPLN. INFO.:			US 1999-159674P	P 19991015
			US 2000-185587P	P 20000228
			WO 2000-US28468	W 20001013

AB An injectable formulation is disclosed for delivery of osteogenic proteins. The formulation comprises a ~~pharmaceutically acceptable admixt.~~ of an osteogenic protein; and formulations comprising osteogenic protein, hyaluronic acid derivs. and tricalcium phosphate are also disclosed. Methods for formulating porous injectable gels and pastes from hyaluronic acid are also disclosed. Hyaff-11p80 was solubilized in N-methylpyrrolidinone, then mixed with RhBMP-2-contg. buffer (0.1 mg/mL) followed by addn. of various pore formers (like sodium bicarbonate) and tricalcium phosphate. In vitro release kinetics of the rhBMP-2 was studied.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:763921 CAPLUS

DOCUMENT NUMBER: 132:6391

TITLE: Biomaterials containing hyaluronic acid derivatives in the form of three-dimensional structures free from cellular components or products thereof, for the in vivo regeneration of tissue cells

INVENTOR(S): **Pavesio, Alessandra;** Dona', Massimo;  
**Callegaro, Lanfranco**

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.L., Italy

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961080	A1	19991202	WO 1999-EP3604	19990525
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
IT 1302535	B1	20000905	IT 1998-PD299	19981221
CA 2332532	AA	19991202	CA 1999-2332532	19990525
AU 9943680	A1	19991213	AU 1999-43680	19990525
AU 748303	B2	20020530		
EP 1085917	A1	20010328	EP 1999-926410	19990525
EP 1085917	B1	20021113		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI			
JP 2002516154	T2	20020604	JP 2000-550539	19990525
AT 227589	E	20021115	AT 1999-926410	19990525
ES 2184460	T3	20030401	ES 1999-926410	19990525
PRIORITY APPLN. INFO.:			IT 1998-PD131	A 19980527
			IT 1998-PD299	A 19981221
			WO 1999-EP3604	W 19990525

AB Use of biocompatible biomaterials contg. hyaluronic acid derivs., with three-dimensional structures enclosing hollow spaces created by communicating pores and/or entangled fine, fibers or microfibres, free from cellular components or products thereof for the in vivo regeneration of tissue cells is disclosed. The tissue obtained by this regeneration, has the same structure, functions as the corresponding natural tissue and is well integrated in the adjacent tissue cells. Benzyl ester of hyaluronic acid (65% esterification) was implanted in bones of rats paws. After 24 days the ester induced a greater degree of bone regeneration than the total benzyl ester or hyaluronic acid in powder form.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:325821 CAPLUS

DOCUMENT NUMBER: 130:343033

TITLE: Ester derivatives of hyaluronic acid with viscoelastic properties and their use in the biomedical and health care field

INVENTOR(S): Renier, Davide; Pavesio, Alessandra; Callegaro, Lanfranco

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers, S.r.L., Italy

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9924070 A2 19990520 WO 1998-EP7020 19981105

WO 9924070 A3 19990715

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9915598 A1 19990531 AU 1999-15598 19981105

PRIORITY APPLN. INFO.:

IT 1997-PD253 19971106  
 WO 1998-EP7020 19981105

AB Viscoelastic compns. are described comprised of esters of hyaluronic acid which are uniquely advantageous because their viscoelastic characteristics may vary according to shearing stress and temp. Pr, Bu, benzyl, and octyl esters of hyaluronic acid were prepd. from tetrabutylammonium hyaluronate and the appropriate alkyl (or benzyl) bromide.

L3 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:265578 CAPLUS

DOCUMENT NUMBER: 126:255537

TITLE: Biomaterials for preventing post-surgical adhesions comprised of hyaluronic acid derivatives

INVENTOR(S): Pressato, Daniele; Pavesio, Alessandra; Callegaro, Lanfranco

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers, S.R.L., Italy; Pressato, Daniele; Pavesio, Alessandra; Callegaro, Lanfranco

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9707833	A2	19970306	WO 1996-EP3805	19960829
WO 9707833	A3	19970410		
W:		AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM		
CA 2230530	AA	19970306	CA 1996-2230530	19960829
AU 9669300	A1	19970319	AU 1996-69300	19960829
AU 718484	B2	20000413		
EP 850074	A2	19980701	EP 1996-930132	19960829
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI		
CN 1199343	A	19981118	CN 1996-197522	19960829
BR 9610996	A	19990713	BR 1996-10996	19960829
JP 11511344	T2	19991005	JP 1996-509858	19960829
RU 2177332	C2	20011227	RU 1998-105612	19960829
NO 9800888	A	19980427	NO 1998-888	19980227

PRIORITY APPLN. INFO.:

IT 1995-PD166 A 19950829  
 IT 1995-PD167 A 19950829  
 WO 1996-EP3805 W 19960829

AB New biomaterials essentially constituted by esterified derivs. of hyaluronic acid or by crosslinked derivs. of hyaluronic acid for use in the surgical sector, particularly for use in the prevention of



post-surgical adhesions, are provided. A soln. of hyaluronic acid benzyl ester in DMSO at 135 mg/mL was prepd. and fed into a spinneret for wet extrusion and the extruded mass of threads was passed into a coagulation bath contg. abs. ethanol. The hank of threads was blown dry and cut into 40 mm fibers, which were made into a web. The web was then sprayed with a soln. of hyaluronic acid benzyl ester in DMSO at 80 mg/mL, placed in an ethanol coagulation bath, in a rinsing chamber, and lastly in a drying chamber, to give a nonwoven fabric with a thickness of 0.5 mm.

=> fil capl; d que 137; d que 139; d que 141; d que 142; d que 145; d que 148; d que 178

FILE 'CAPLUS' ENTERED AT 17:10:53 ON 02 FEB 2004  
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FILE COVERS 1907 - 2 Feb 2004 VOL 140 ISS 6  
FILE LAST UPDATED: 1 Feb 2004 (20040201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L33 139 SEA FILE=CAPLUS ABB=ON L32  
L36 87410 SEA FILE=CAPLUS ABB=ON VIVO/OBI  
L37 2 SEA FILE=CAPLUS ABB=ON L33 AND L36

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER  
L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L36 87410 SEA FILE=CAPLUS ABB=ON VIVO/OBI  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L39 1 SEA FILE=CAPLUS ABB=ON L38 AND L36

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER  
L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L13 27180 SEA FILE=CAPLUS ABB=ON PROSTHETIC#/CW  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L40 2 SEA FILE=CAPLUS ABB=ON L38 (L) TEM/RL - Role - Technical or Engineering Material  
L41 1 SEA FILE=CAPLUS ABB=ON L40 AND L13

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER

L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L15 8660 SEA FILE=CAPLUS ABB=ON NONWOVEN FABRICS/CT  
L17 25716 SEA FILE=CAPLUS ABB=ON HOLLOW/OBI  
L18 47729 SEA FILE=CAPLUS ABB=ON PORE#/OBI  
L19 163 SEA FILE=CAPLUS ABB=ON (TANGL?/OBI OR ENTANGL?/OBI) (L) (FIBER#/  
OBI OR FIBRE#/OBI OR MICROFIBRE#/OBI OR MICROFIBER#/OBI)  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L33 139 SEA FILE=CAPLUS ABB=ON L32  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L42 6 SEA FILE=CAPLUS ABB=ON (L38 OR L33) AND (L15 OR (L17 OR L18  
OR L19))

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER  
L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L12 24074 SEA FILE=CAPLUS ABB=ON MEDICAL GOODS/CT  
L13 27180 SEA FILE=CAPLUS ABB=ON PROSTHETIC#/CW  
L16 49502 SEA FILE=CAPLUS ABB=ON 3D/OBI OR (3/OBI OR THREE/OBI) (W) (DIMEN  
SION?/OBI OR D/OBI)  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L33 139 SEA FILE=CAPLUS ABB=ON L32  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L44 6 SEA FILE=CAPLUS ABB=ON (L12 OR L13) AND (L38 OR L33) AND L16  
L45 5 SEA FILE=CAPLUS ABB=ON L44 NOT SUPERCRITICAL/TI

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER  
L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L12 24074 SEA FILE=CAPLUS ABB=ON MEDICAL GOODS/CT  
L13 27180 SEA FILE=CAPLUS ABB=ON PROSTHETIC#/CW  
L20 4852 SEA FILE=CAPLUS ABB=ON BIOLOGICAL MATERIALS/CT  
L21 20760 SEA FILE=CAPLUS ABB=ON MEMBRANES, NONBIOLOGICAL/CT  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L33 139 SEA FILE=CAPLUS ABB=ON L32  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L48 4 SEA FILE=CAPLUS ABB=ON (L12 OR L13 OR PHARMAC?/SC, SX) AND  
((L20 OR L21)) AND (L38 OR L33)

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L7 130 SEA FILE=REGISTRY ABB=ON L6 AND ESTER  
L8 82 SEA FILE=CAPLUS ABB=ON L5/D(L)ESTER?/OBI  
L9 271 SEA FILE=CAPLUS ABB=ON L7  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L33 139 SEA FILE=CAPLUS ABB=ON L32  
L38 74 SEA FILE=CAPLUS ABB=ON (L8 OR L9) (L) BENZYL?/OBI  
L66 1130190 SEA FILE=CAPLUS ABB=ON (POLYMER#/OBI OR BIOPOLYMER#/OBI)  
L75 14318 SEA FILE=CAPLUS ABB=ON (SEMISYNTHETIC/OBI OR SYNTHETIC/OBI OR

NATURAL/OBI) (2A) L66  
L77 10380 SEA FILE=CAPLUS ABB=ON BIOPOLYMER#/OBI  
L78 6 SEA FILE=CAPLUS ABB=ON (L75 OR L77) AND (L38 OR L33)

=> s (l37 or l39 or l41 or l42 or l45 or l48 or l78) not l3

L121 21 (L37 OR L39 OR L41 OR L42 OR L45 OR L48 OR L78) NOT L3

*printed w/  
inventor search*

=> fil uspatf; d que 162; d que 163; d que 165

FILE 'USPATFULL' ENTERED AT 17:10:54 ON 02 FEB 2004  
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 29 Jan 2004 (20040129/PD)  
FILE LAST UPDATED: 29 Jan 2004 (20040129/ED)  
HIGHEST GRANTED PATENT NUMBER: US6684403  
HIGHEST APPLICATION PUBLICATION NUMBER: US2004019947  
CA INDEXING IS CURRENT THROUGH 29 Jan 2004 (20040129/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 29 Jan 2004 (20040129/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2003  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2003

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>>> publications, starting in 2001, for the inventions covered in <<<  
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L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L49 31 SEA FILE=USPATFULL ABB=ON L32 OR L5(L)ESTER?/IT(L)BENZYL?/IT  
L52 12780 SEA FILE=USPATFULL ABB=ON VIVO/IT, TI, CLM, AB  
L62 1 SEA FILE=USPATFULL ABB=ON L49 AND L52

L5 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN  
L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
L49 31 SEA FILE=USPATFULL ABB=ON L32 OR L5(L)ESTER?/IT(L)BENZYL?/IT  
L51 16149 SEA FILE=USPATFULL ABB=ON (NONWOVEN OR NON WOVEN)/IT, TI, CLM, AB

L53 7083 SEA FILE=USPATFULL ABB=ON MEDICAL GOODS/CT  
 L54 11852 SEA FILE=USPATFULL ABB=ON PROSTHE?/IT, TI, CLM, AB  
 L55 39334 SEA FILE=USPATFULL ABB=ON (3D OR (3 OR THREE) (W) (DIMENSION?  
 OR D)) /IT, TI, CLM, AB  
 L56 188362 SEA FILE=USPATFULL ABB=ON (HOLLOW OR PORE#) /IT, TI, CLM, AB  
 L57 819 SEA FILE=USPATFULL ABB=ON ((TANGL? OR ENTANGL?) (3A) (FIBRE# OR  
 FIBER# OR MICROFIBER# OR MICRO FIBER#)) /IT, TI, CLM, AB  
 L58 808 SEA FILE=USPATFULL ABB=ON BIOLOGICAL MATERIALS/CT  
 L59 2799 SEA FILE=USPATFULL ABB=ON MEMBRANES, NONBIOLOGICAL/CT  
 L63 8 SEA FILE=USPATFULL ABB=ON L49 AND L51 AND (L53 OR L54 OR L55  
 OR L56 OR L57 OR L58 OR L59)

L5 1 SEA FILE=REGISTRY ABB=QN "HYALURONIC ACID"/CN  
 L6 304 SEA FILE=REGISTRY ABB=ON 9004-61-9/CRN  
 L31 745 SEA FILE=REGISTRY ABB=ON 100-51-6/CRN  
 L32 27 SEA FILE=REGISTRY ABB=ON L6 AND L31  
 L49 31 SEA FILE=USPATFULL ABB=ON L32 OR L5(L) ESTER?/IT(L) BENZYL?/IT  
 L53 7083 SEA FILE=USPATFULL ABB=ON MEDICAL GOODS/CT  
 L54 11852 SEA FILE=USPATFULL ABB=ON PROSTHE?/IT, TI, CLM, AB  
 L58 808 SEA FILE=USPATFULL ABB=ON BIOLOGICAL MATERIALS/CT  
 L64 211671 SEA FILE=USPATFULL ABB=ON (POLYMER# OR BIOPOLYMER#) /IT, TI, AB, C  
 LM  
 L65 6 SEA FILE=USPATFULL ABB=ON L49 AND L64 AND (L53 OR L54 OR L58)

=> s 162 or 163 or 165

L122 10 L62 OR L63 OR L65

=> fil medl; d que 190; d que 192

FILE 'MEDLINE' ENTERED AT 17:10:55 ON 02 FEB 2004

FILE LAST UPDATED: 31 JAN 2004 (20040131/UP). FILE COVERS 1958 TO DATE.

On December 14, 2003, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and [http://www.nih.gov/pubs/yechebull/nd03/nd03\\_mesh.html](http://www.nih.gov/pubs/yechebull/nd03/nd03_mesh.html) for a description on changes.

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L81 7609 SEA FILE=MEDLINE ABB=ON HYALURONIC ACID/CT  
 L83 1689 SEA FILE=MEDLINE ABB=ON ESTERIFICATION/CT  
 L86 8983 SEA FILE=MEDLINE ABB=ON ESTERS/CT  
 L87 17883 SEA FILE=MEDLINE ABB=ON BIOCOMPATIBLE MATERIALS/CT  
 L90 5 SEA FILE=MEDLINE ABB=ON L81 AND (L83 OR L86) AND L87

L81 7609 SEA FILE=MEDLINE ABB=ON HYALURONIC ACID/CT  
 L83 1689 SEA FILE=MEDLINE ABB=ON ESTERIFICATION/CT  
 L86 8983 SEA FILE=MEDLINE ABB=ON ESTERS/CT  
 L88 13 SEA FILE=MEDLINE ABB=ON L81 AND (L83 OR L86)

L91 33197 SEA FILE=MEDLINE ABB=ON ?BENZYL? OR PHENYLMETHYL OR PHENYL  
METHYL

L92 4 SEA FILE=MEDLINE ABB=ON L88 AND L91

=> s l90 or l92

L123 6 L90 OR L92

=> fil embase; d que l94; d que l104; d que l105

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L94 4 SEA FILE=EMBASE ABB=ON HYALURONIC ACID BENZYL ESTER/CT

L93 8247 SEA FILE=EMBASE ABB=ON HYALURONIC ACID/CT

L95 3226 SEA FILE=EMBASE ABB=ON ESTER/CT

L96 3826 SEA FILE=EMBASE ABB=ON ESTERIFICATION/CT

L101 223 SEA FILE=EMBASE ABB=ON HYALURONIC ACID DERIVATIVE/CT

L102 2128 SEA FILE=EMBASE ABB=ON BENZYL ALCOHOL/CT OR BENZYL DERIVATIVE/  
CT

L104 3 SEA FILE=EMBASE ABB=ON (L93 OR L101) AND (L95 OR L96) AND  
L102

=> d que l105

L93 8247 SEA FILE=EMBASE ABB=ON HYALURONIC ACID/CT

L95 3226 SEA FILE=EMBASE ABB=ON ESTER/CT

L96 3826 SEA FILE=EMBASE ABB=ON ESTERIFICATION/CT

L98 51507 SEA FILE=EMBASE ABB=ON ?BENZYL? OR PHENYLMETHYL OR PHENYL  
METHYL

L101 223 SEA FILE=EMBASE ABB=ON HYALURONIC ACID DERIVATIVE/CT

L103 6180 SEA FILE=EMBASE ABB=ON BIOMATERIAL/CT

L105 5 SEA FILE=EMBASE ABB=ON (L93 OR L101) AND (L95 OR L96) AND L98  
AND L103

=> s l94 or l104 or l105

L124 11 L94 OR L104 OR L105

=> fil DRUGU, PASCAL, BIOTECHNO, BIOSIS, TOXCENTER, SCISEARCH

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=> d que 1119; d que 1120

L107 43603 SEA HYALURON?  
L108 831980 SEA ESTER?  
L109 249813 SEA ?BENZYL? OR PHENYLMETHYL OR PHENYL METHYL  
L110 143 SEA L107(5A) L108(8A) L109  
L111 4455 SEA NONWOVEN OR NON WOVEN  
L118 17 SEA L110 AND L111  
L119 11 DUP REM L118 (6 DUPLICATES REMOVED)

L107 43603 SEA HYALURON?  
L108 831980 SEA ESTER?  
L109 249813 SEA ?BENZYL? OR PHENYLMETHYL OR PHENYL METHYL  
L110 143 SEA L107(5A) L108(8A) L109  
L112 247 SEA ((TANGL? OR ENTANGL?) (3A) (FIBRE# OR FIBER# OR MICROFIBER#  
OR MICRO FIBER#))  
L113 44520 SEA HOLLOW  
L114 174431 SEA PORE#  
L120 5 SEA L110 AND (L112 OR L113 OR L114)

=> s 1119 or 1120

L125 16 L119 OR L120

=> dup rem 1123,1121,1124,1125,1122

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PROCESSING COMPLETED FOR L121  
PROCESSING COMPLETED FOR L124  
PROCESSING COMPLETED FOR L125  
PROCESSING COMPLETED FOR L122

L126 55 DUP REM L123 L121 L124 L125 L122 (9 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE MEDLINE  
ANSWERS '7-27' FROM FILE CAPLUS  
ANSWERS '28-36' FROM FILE EMBASE  
ANSWER '37' FROM FILE DRUGU  
ANSWER '38' FROM FILE PASCAL  
ANSWERS '39-40' FROM FILE BIOTECHNO  
ANSWERS '41-45' FROM FILE TOXCENTER  
ANSWER '46' FROM FILE SCISEARCH  
ANSWERS '47-55' FROM FILE USPATFULL

=> d ibib ab 1-6; d ibib ab hitrn 7-27; d ibib ab 28-46; d ibib ab hitrn 47-55; fil hom

L126 ANSWER 1 OF 55 MEDLINE on STN DUPLICATE 6  
ACCESSION NUMBER: 1999098521 MEDLINE  
DOCUMENT NUMBER: 99098521 PubMed ID: 9884052  
TITLE: Semisynthetic resorbable materials from hyaluronan esterification.  
AUTHOR: Campoccia D; Doherty P; Radice M; Brun P; Abatangelo G; Williams D F  
CORPORATE SOURCE: Fidia Advanced Biopolymers, Albano Terme (PD), Italy.  
SOURCE: BIOMATERIALS. (1998; Dec) 19 (23) 2101-27. Ref: 174  
Journal code: 8100316. ISSN: 0142-9612.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199904  
ENTRY DATE: Entered STN: 19990413  
Last Updated on STN: 19990413  
Entered Medline: 19990401

AB In recent years, research on new, biocompatible, degradable materials has seen the development of a series of modified natural polymers. Among these, a new class of materials consisting of different hyaluronan derivatives promises to be useful in a whole range of clinical applications thanks to their varied biological properties. These new materials are obtained by chemical modification of purified hyaluronan consisting of the partial or total esterification of the carboxyl groups of this natural polymer. This review on the properties of the new materials reports some of their biocompatibility and characterization aspects based on findings from studies conducted on the ethyl and **benzyl** hyaluronan esters, two representative members of this new class of compounds, and is intended to arouse interest in the potential of other, as yet unexplored derivatives. From the results of a number of investigations, the various derivatives appear to possess different physico-chemical properties, especially as far as the degree of hydration



and polymer stability are concerned. In addition, the type of esterification and extent of chemical esterification of hyaluronan considerably affects the biological properties of these materials, offering a range of polymers either favouring or, conversely, inhibiting the adhesion of certain types of cell.

L126 ANSWER 2 OF 55 MEDLINE on STN DUPLICATE 7  
ACCESSION NUMBER: 94339266 MEDLINE  
DOCUMENT NUMBER: 94339266 PubMed ID: 8061127  
TITLE: Biodegradation of hyaluronic acid derivatives by hyaluronidase.  
AUTHOR: Zhong S P; Campoccia D; Doherty P J; Williams R L; Benedetti L; Williams D F  
CORPORATE SOURCE: Department of Clinical Engineering, University of Liverpool, UK.  
SOURCE: BIOMATERIALS, (1994 Apr) 15 (5) 359-65.  
Journal code: 8100316. ISSN: 0142-9612.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199409  
ENTRY DATE: Entered STN: 19941005  
Last Updated on STN: 19980206  
Entered Medline: 19940922

AB Hyaluronic acid (salt) (HA) has been chemically modified as a biomaterial for medical applications such as controlled drug release matrices, nerve guides and wound dressings. A series of HA derivatives, which include different ester types and different degrees of esterification, have been used to investigate the stability of these materials in testicular hyaluronidase. Gel permeation chromatography and capillary viscometer have been employed to determine the size of the molecules, the former used for the water insoluble derivatives that dissolve in dimethyl sulphoxide, the latter for the water soluble samples. The preliminary experimental results indicated that the molecular weight of fully esterified hyaluronic acid (both ethyl and benzyl esters) did not decrease after treatment in the enzyme for 7 and 14 days while the water soluble partially esterified HA were degraded by the enzyme producing a sharp reduction of viscosity within minutes. These observations tend to suggest that the carboxylic groups in the beta-glucuronic acid unit are the activation centre of this enzyme and the total blockage of these groups can restrict the cleavage of beta (1-->4) glycoside bonds by this enzyme.

L126 ANSWER 3 OF 55 MEDLINE on STN  
ACCESSION NUMBER: 2001293641 MEDLINE  
DOCUMENT NUMBER: 21244332 PubMed ID: 11346429  
TITLE: Evaluation of esterified hyaluronic acid as middle ear-packing material.  
AUTHOR: Li G; Feghali J G; Dinces E; McElveen J; van de Water T R  
CORPORATE SOURCE: Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY 10461, USA.  
SOURCE: ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (2001 May) 127 (5) 534-9.  
Journal code: 8603209. ISSN: 0886-4470.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 20010604  
Last Updated on STN: 20010604  
Entered Medline: 20010531  
AB OBJECTIVE: To evaluate the efficacy of esterified hyaluronic acid

(MeroGel) as a middle ear (ME)-packing material. DESIGN: Randomized controlled trial. MATERIAL: Twenty-four guinea pigs. INTERVENTION: Group 1, MeroGel-treated animals (n = 10), bilateral wounding of ME mucosa with 5 of the animals receiving the MeroGel packing in the left ME and 5 of the animals receiving MeroGel in the right ME; group 2, absorbable gelatin sponge-treated animals (n = 10), with the same experimental protocol as in group 1 except that the absorbable gelatin sponge was the packing material; group 3, untreated animals (n = 4), unilateral wounding of the left ME mucosa in 2 animals and in 2 animals in the right ME, with no packing material. Auditory brainstem recordings were performed for all groups before the ME operation and 5 days and 6 weeks after the operation. RESULTS: Auditory brainstem response recordings at postoperative day 5 showed that all ears with ME packing had hearing losses in the frequency range of 500 to 4000 Hz. The recovery of hearing acuity at postoperative week 6 was significantly better in group 1 (MeroGel-treated) guinea pigs compared with group 2 (the absorbable gelatin sponge-treated) animals. In group 2 animals, 20% of the packing material remained in the ME cavities and new bone formation was observed, while in group 1 animals, there was less packing material in the ME and no formation of new bone. CONCLUSIONS: MeroGel is a nonototoxic packing material with a high level of biocompatibility for ME mucosa; it is an effective supportive material following ME surgery and is easily expelled from the ME cavity.

L126 ANSWER 4 OF 55 MEDLINE on STN  
ACCESSION NUMBER: 96440059 MEDLINE  
DOCUMENT NUMBER: 96440059 PubMed ID: 8842370  
TITLE: Application of **benzyl** hyaluronate membranes as potential wound dressings: evaluation of water vapour and gas permeabilities.  
AUTHOR: Ruiz-Cardona L; Sanzgiri Y D; Benedetti L M; Stella V J; Topp E M  
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kansas, Lawrence 66045, USA.  
SOURCE: BIOMATERIALS, (1996 Aug) 17 (16) 1639-43.  
Journal code: 8100316. ISSN: 0142-9612.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199612  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19961230

AB Membranes of 75% and 100% **benzyl** hyaluronate esters (percentage of total carboxylate groups esterified) were prepared and their water vapour, oxygen and carbon dioxide transmission rates determined. The values of these properties were compared with the values obtained for several commercial wound dressings under the same conditions. The **benzyl** hyaluronate membranes showed water vapour transmission rates (2157-2327 gm<sup>-2</sup> per day) comparable to those from commercial skin dressings (426-2047 gm<sup>-2</sup> per day). In the dry state, the **benzyl** hyaluronate membranes showed lower oxygen and carbon dioxide transmission rates. Taking into account the biocompatibility of the hyaluronic acid esters, and the possibility that therapeutic agents could be incorporated into these membranes, the results indicate that the **benzyl** hyaluronate membranes have potential wound dressing applications.

L126 ANSWER 5 OF 55 MEDLINE on STN  
ACCESSION NUMBER: 92379807 MEDLINE  
DOCUMENT NUMBER: 92379807 PubMed ID: 1511449  
TITLE: 1H- and 13C-NMR studies of solutions of hyaluronic acid esters and salts in methyl sulfoxide: comparison of hydrogen-bond patterns and conformational behaviour.

AUTHOR: Kvam B J; Atzori M; Toffanin R; Paoletti S; Biviano F  
CORPORATE SOURCE: POLY-bios Research Centre, LBT--Area di Ricerca, Trieste, Italy.  
SOURCE: CARBOHYDRATE RESEARCH, (1992 Jun 4) 230 (1) 1-13.  
Journal code: 0043535. ISSN: 0008-6215.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199210  
ENTRY DATE: Entered STN: 19921018  
Last Updated on STN: 19921018  
Entered Medline: 19921001

AB The <sup>1</sup>H- and <sup>13</sup>C-NMR spectra of the ethyl and **benzyl** esters and the tetrabutylammonium and tetraethylammonium salts of hyaluronic acid [[symbol: see text]2)-beta-D-GcpA+-1----3)-beta-D-GlcpNAc-(1[symbol: see text]n) in Me<sub>2</sub>SO-d<sub>6</sub> have been assigned using 1D and 2D techniques. The chemical shifts of the resonance of GlcNAc C-3 suggest that the relative orientations of the monosaccharides at the (1----3) linkage in the esters and salts are different. Small differences in the chemical shifts of the resonance GlcA C-4 suggest only a slight conformational variation around the (1---4) linkage. The <sup>13</sup>C-NMR data also suggest similarities in conformation between the esters in Me<sub>2</sub>SO-d<sub>6</sub> and the salts in water. The chemical shifts of the <sup>1</sup>H resonances for NH and OH groups and their temperature dependence for the esters and salts in Me<sub>2</sub>SO reveal markedly stronger inter-residue hydrogen bonds between the carboxyl and NH groups and between HO-4 of GlcA and O-5 of GlcNAc for the salts. The 3J<sub>2,NH</sub> values indicate a slightly different orientation for the acetamido group. For solutions in Me<sub>2</sub>SO, the higher segmental flexibility of the esters is supported by the line widths, whereas the reduced viscosity for the tetrabutylammonium salt showed a sigmoidal concentration dependence and suggests association of chains which could contribute to the segmental rigidity. The linear concentration dependence for the **benzyl** ester suggests a higher overall flexibility without chain association.

L126 ANSWER 6 OF 55 MEDLINE on STN  
ACCESSION NUMBER: 92190407 MEDLINE  
DOCUMENT NUMBER: 92190407 PubMed ID: 1799648  
TITLE: In vitro studies on biocompatibility of hyaluronic acid esters.  
AUTHOR: Cortivo R; Brun P; Rastrelli A; Abatangelo G  
CORPORATE SOURCE: Institute of Histology, University of Padova, Italy.  
SOURCE: BIOMATERIALS, (1991 Oct) 12 (8) 727-30.  
Journal code: 8100316. ISSN: 0142-9612.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199204  
ENTRY DATE: Entered STN: 19920509  
Last Updated on STN: 19920509  
Entered Medline: 19920421

AB The biocompatibility of semisynthetic polymers formed from hyaluronic acid esters has been studied using fibroblast cultures. The polymers, added to the culture medium, used either in powdered form or as thin membranes, behave as inert materials. The cells used in the experiments grow normally in the culture dishes. With regard to adhesiveness the cells were not able to spread on the biomembranes and tended to form isolated clusters of round cells. Human fibronectin, placental collagen (type I-IV) and fibrin could be stratified on biomembranes. When these molecules reacted with the biomaterial the film became suitable for fibroblasts spreading and growth.

L126 ANSWER 7 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4  
ACCESSION NUMBER: 2000:724680 CAPLUS  
DOCUMENT NUMBER: 134:32921  
TITLE: Chemico-physical properties of hyaluronan-based sponges  
AUTHOR(S): Milella, E.; Brescia, E.; Massaro, C.; Ramires, P. A.  
CORPORATE SOURCE: Biomaterials Unit, PASTIS-CNRSM, Brindisi, Italy  
SOURCE: Journal of Biomedical Materials Research (2000), 52(4), 695-700  
CODEN: JBMRBG; ISSN: 0021-9304  
PUBLISHER: John Wiley & Sons, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The aim of this study was to obtain information on the chemico-phys. and surface properties of the hyaluronan total benzylic ester sponges to evaluate their stability, surface "cleanliness" and handling for the applications in the tissue engineering. The thermal anal., the characterization of surface chem. compn. and the swelling test were performed on these materials. Moreover, the morphol. changes, the rheol. behavior, and the mol. wt. loss in function of the time were monitored when the sponges were incubated in cell culture medium. The results showed that the sponges were thermally stable up to 220.degree.C and the surface compn. was different from that of the bulk for C-O contribution. No contaminants were detected. In culture medium, the samples swelled assuming the rheol. properties of biopolymer gel. When the sponges were in contact with the culture medium, their mol. wt. remained stable for the first day and a loss of 11% and 31% was recorded for samples removed from culture medium after 3 and 7 days, resp. With the SEM anal., the spongy structure appeared with open interconnecting pores. The micrographs related to the samples after incubation in culture medium showed that the degrdn. was evident on the surface after 1 day. The deterioration of the pore walls and the presence of craters increased with time and, after 3 days, the phenomena were present also in the section.

IT 111744-92-4, HYAFF 11  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(physicochem. properties of hyaluronan-based sponges for biomaterials)  
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 8 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:666708 CAPLUS  
DOCUMENT NUMBER: 140:43256  
TITLE: Hydrophobic/hydrophilic electrospun membranes for biomedical applications  
AUTHOR(S): Jiang, H. L.; Fang, D. F.; Hsiao, B.; Chu, B.; Chen, W.  
CORPORATE SOURCE: Department of Biomedical Engineering, State University of New York at Stony Brook, NY, 11794-2580, USA  
SOURCE: Polymeric Materials Science and Engineering (2003), 89, 350  
CODEN: PMSEDG; ISSN: 0743-0515  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal; (computer optical disk)  
LANGUAGE: English

AB Ethylene glycol-chitosan graft copolymer, hyaluronan benzyl ester, dextran, lactide-glycolide copolymer, and their blends are electrospun to obtain porous membrane with uniform nanofibrous structure that can be used for biomedical applications.

IT 111744-92-4, Hyaluronan **benzyl** ester

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(hydrophobic/hydrophilic electrospun membranes for biomedical applications)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 9 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:9664 CAPLUS

DOCUMENT NUMBER: 138:193161

TITLE: Soft tissue reconstruction in severely traumatized patients using hyaluronan based dermal and epidermal grafts

AUTHOR(S): Hollander, Dirk A.; Kraemer, Susanne; Hakimi, Mohssen Y.; Windolf, Joachim

CORPORATE SOURCE: Department of Trauma and Reconstructive Surgery, Johann Wolfgang Goethe-University, Frankfurt/Main, 60590, Germany

SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 87-98. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK. CODEN: 69DKVZ; ISBN: 1-85573-570-9

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Background: This report demonstrates the potential of two-stage autologous keratodermal grafting as a starting point for non-invasive reconstruction of extensive traumatic soft-tissue defects. Methods: In severely injured patients skin biopsies for cell cultivation were taken. Cultured "neodermis" consisting of cultured autologous fibroblasts grown on biocompatible three-dimensional scaffolds made up of benzylester of hyaluronan was grafted on conditioned defect areas. After ingrowth of dermal substitutes transplantation of cultured autologous keratinocytes on hyaluronan based laser-perforated membranes was performed. 10 Days later a 0.2 mm thin, 1:6 meshed autograft was overlaid. Clin. follow-up with std. photog. was documented. Results: Grafting with cultured autologous fibroblasts revealed a suitable dermal tissue replacement. Epithelialization was evident after transplantation of keratinocytes. Final closure of the defects with normo-elastic tissue properties was achieved after thin mesh-grafting. Conclusions: Preliminary findings with the described method seem to be very promising. As in all fields of tissue engineering, long-term studies and further follow-up are required.

IT 111744-92-4, Hyalograft 3d

RL: BSU (Biological study, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(soft tissue reconstruction in severely traumatized patients using hyaluronan based dermal and epidermal grafts)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 10 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:9663 CAPLUS

DOCUMENT NUMBER: 138:61259

TITLE: Hyaluronan based dermal and epidermal grafts in the treatment of diabetic foot ulcers

AUTHOR(S): Caravaggi, Carlo; Faglia, Ezio; Dalla Paola, Luca; Clerici, Giacomo; De Giglio, Roberto; Sommariva, Emanuela; Pritelli, Chiara; Mantero, Manuela; Caminiti, Maurizio; Curci, Vincenzo; Fratino, Pietro

CORPORATE SOURCE: Presidio Ospedaliero C. Cantu, Centre for the Study and Treatment of Diabetic Foot Pathology, Abbiategrasso (MI), 20080, Italy

SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 79-86. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK. CODEN: 69DKVZ; ISBN: 1-85573-570-9

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The normal healing process of ulcers is often impaired in diabetic patients, thus, contributing to the pathophysiol. that ultimately leads to amputation. Recently, great interest has been given to the use of tissue engineering for the treatment of such problematic ulcers. This approach involves the in vitro prodn. of tissues obtained by making specific cells proliferate on three-dimensional polymeric scaffolds able to support their growth and the prodn. of components of the extracellular matrix. HYAFF scaffolds have been employed to produce hyaluronan based tissue engineered skin grafts. The dermal component of the skin has been addressed by using a three-dimensional HYAFF fiber mesh scaffold, named Hyalograft 3D, designed to support fibroblast cultures. Epithelialization is achieved by employing autologous keratinocyte grafts delivered on Laserskin, a HYAFF microperforated transparent membrane designed to facilitate graft handling procedures and to enable grafting at preconfluence. The results of uncontrolled and controlled clin. studies involving the use of a two stage dermo-epidermal autologous grafting procedure on diabetic foot ulcers will be reported.

IT 111744-92-4, Hyalograft 3D

RL: BSU (Biological study, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hyaluronan based dermal and epidermal grafts in treatment of patients with diabetic foot ulcers)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 11 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:816510 CAPLUS

DOCUMENT NUMBER: 135:348862

TITLE: Biomaterials comprised of preadipocyte cells for soft tissue repair

INVENTOR(S): Von Heimburg, Dennis; Pavesio, Alessandra

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Italy

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082991	A2	20011108	WO 2001-EP5087	20010503
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1280562	A2	20030205	EP 2001-940405	20010503
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003531684	T2	20031028	JP 2001-579862	20010503

## PRIORITY APPLN. INFO.:

US 2000-201984P P 20000503  
WO 2001-EP5087 W 20010503

- AB Biomaterials are described comprised of a scaffold support or injectable material comprising a benzyl ester of and/or an amide of hyaluronic acid having adipocytes, mesenchymal stem cells and/or endothelial cells disposed thereon, and which are useful in reconstructive surgery for correction of soft tissue damage.
- IT **111744-92-4, Benzyl** hyaluronate  
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(biomaterials comprised of preadipocyte cells for soft tissue repair)
- L126 ANSWER 12 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:400673 CAPLUS  
DOCUMENT NUMBER: 135:247157  
TITLE: Production of different morphologies of biocompatible polymeric materials by supercritical CO2 antisolvent techniques  
AUTHOR(S): Elvassore, Nicola; Baggio, Marco; Pallado, Paolo; Bertucco, Alberto  
CORPORATE SOURCE: Department of Chemical Engineering Principles and Equipment, Universita di Padova, Padua, I-35131, Italy  
SOURCE: Biotechnology and Bioengineering (2001), 73(6), 449-457  
CODEN: BIBIAU; ISSN: 0006-3592  
PUBLISHER: John Wiley & Sons, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English
- AB High-value biocompatible-polymers have been processed with supercrit. antisolvent techniques to produce solid structures of different shape and size. In particular, a class of hyaluronic acid-derived polymers (Hyaff 11p50, Hyaff 11p80, Hyaff 11p75, Hyaff 302) have been used to obtain various morphologies such as microspheres, threads, fibers; networks, and sponges. The effect of thermodyn. variables on pptn. were highlighted in some preliminary batch expts. Then, different products were obtained by tuning the values of operating parameters. Threads and fibers were the result of a continuous supercrit. antisolvent (SAS) process where a concd. polymer soln. was pumped through a micrometric nozzle: The threads showed a reticular internal structure with an adjustable type of cavity. For prodn. of networks and sponges, the concn. of polymer plays the key role. Below a crit. value it was not possible to obtain a continuous network, while above it, a structure similar to that of the natural bone with three types of internal microporosity were obtained. Again, by tuning pressure and polymer concn., the internal porosity could be controlled. Microparticles were also produced by the SAS process, and a control of their morphol. was achieved by varying the concn. of the polymer in the starting soln. and the d. of org. solvent-CO2 mixts. All the products obtained by SAS have negligible content of residual solvent. A qual. interpretation of exptl. results is presented.
- IT **111744-92-4, Hyaff 11p80**  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Hyaff 11, Hyaff 11p50, Hyaff 11p80; prodn. of different morphol. of biocompatible polymeric materials by supercrit. CO2 antisolvent techniques)
- IT **203874-06-0, Hyaff 302**  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Hyaff 302; prodn. of different morphol. of biocompatible polymeric materials by supercrit. CO2 antisolvent techniques)
- IT **149175-67-7, Hyaff 11p75**  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)

(prodn. of different morphol. of biocompatible polymeric materials by supercrit. CO2 antisolvent techniques)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 13 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:315645 CAPLUS

DOCUMENT NUMBER: 137:375128

TITLE: Intravitreal hyaluronan implants: Biocompatibility and biodegradation in **vivo**

AUTHOR(S): Bucolo, C.; Avitabile, T.; Marano, F.; Castiglione, F.; Cro, M.; Ambrosio, L.; Reibaldi, A.

CORPORATE SOURCE: Fidia Oftal., Laboratori di Ricerca, Catania, Italy  
SOURCE: Acta Technologiae et Legis Medicamenti (2001), 12(2), 179-183

CODEN: ATLMEQ; ISSN: 1121-2098

PUBLISHER: Maccari Editore

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To study the biocompatibility and the biodegrdn. rate of intravitreal implants made with different hyaluronic acid esters, the plugs were implanted in the rabbit eyes. In order to evaluate the in vivo biodegrdn. the shaft diam. of plugs was measured by ultrasound biomicroscopy. Slit lamp microscopy, ophthalmoscopy and ERG were performed periodically. All the plugs showed a good biocompatibility and the biodegrdn. rate of each implant was related to the chem. structure of the esters. The present data suggest that intravitreal hyaluronan implants represent useful biocompatible and biodegradable devices for a potential drug delivery system in the treatment of posterior segment ocular diseases.

IT 111744-92-4, Hyaff 11 149175-67-7, Hyaff 11p75

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(biocompatibility and biodegrdn. of intravitreal hyaluronan implants)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 14 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:384002 CAPLUS

DOCUMENT NUMBER: 133:34465

TITLE: Porous composite matrix based on hyaluronate and hydrolyzed collagen

INVENTOR(S): Angele, Peter; Kujat, Richard

PATENT ASSIGNEE(S): Nerlich, Michael, Germany

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032251	A1	20000608	WO 1999-EP9444	19991203
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,			



CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
DE 19855890 A1 20000608 DE 1998-19855890 19981203  
EP 1135177 A1 20010926 EP 1999-963373 19991203  
EP 1135177 B1 20030604

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

JP 2002531182 T2 20020924 JP 2000-584940 19991203  
AT 242018 E 20030615 AT 1999-963373 19991203

## PRIORITY APPLN. INFO.:

DE 1998-19855890 A 19981203  
WO 1999-EP9444 W 19991203

AB The invention relates to a porous composite matrix, consisting of a hyaluronic acid deriv. and hydrolyzed collagen. The biocompatible and biodegradable composite matrix can be used for tissue engineering of chondral and osseous tissue and for repairing musculoskeletal defects. The composite matrix was obtained by dissolving benzyl hyaluronate and gelatin in 1,1,1,3,3,3-hexafluoroisopropanol, addn. of NaCl crystals and drying the paste. After the removal of NaCl, the composite matrix was sterilized by .gamma.-rays.

IT **111744-92-4, Benzyl Hyaluronate**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(porous composite matrix based on hyaluronate and hydrolyzed collagen)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 15 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:449973 CAPLUS

DOCUMENT NUMBER: 134:61424

TITLE: Tissue engineering in the treatment of diabetic foot ulcers

AUTHOR(S): Caravaggi, Carlo; Faglia, Ezio; Dalla Paola, Luca; De Giglio, Roberto; Cavaiani, Paola; Mantero, Manuela; Gino, Michela; Quarantiello, Antonella; Sommariva, Emanuela; Pritelli, Chiara

CORPORATE SOURCE: Center for the Study and Management of the Diabetic Foot, Abbiategrasso Hospital, Abbiategrasso, 20081, Italy

SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 313-320

CODEN: EXMDA4; ISSN: 0531-5131

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The normal healing process of ulcers is often impaired in diabetic patients, thus, contributing to the pathophysiol. that leads to amputation. Recently, great interest has been given to their treatment with growth factors and allogenic and autologous grafts. Sixty patients were treated with a two-step method of autologous grafting. A nonwoven fleece and a laser microperforated membrane (Hyalograft 3-D and Laserskin, Fidia Advanced Biopolymers, Srl Abano Terme, Italy), both composed entirely of a benzyl ester deriv. of hyaluronic acid (HA), were used as scaffolds for the cultivation of fibroblasts and keratinocytes, resp. All patients were neuropathic. The av. area of the ulcer at enrollment was 616.28 +/- 523.81 mm<sup>2</sup>. Patients with ulcers in the plantar region or heel used a fiberglass pressure relief app., while patients with an ulcer in the dorsal region of the foot wore a fabric shoe with a rigid insole. Autologous fibroblasts were applied after the wound bed was cleansed and aseptic. After approx. 7 days, autologous keratinocytes were applied. Histol. anal. was performed on biopsies taken from 14 patients at day 0 and day 7 following autologous fibroblast application. In an av. time of 72.7 +/- 48.18 days, 91.3% of the patients had complete healing without complications. In all biopsies, the newly formed granulation tissue was characterized by the presence of blood vessels and deposition of collagen

fibers. The high percentage of ulcers completely healed and the low incidence of complications demonstrated that this treatment was efficient and safe for diabetic foot ulcers. The promising results of this pilot study should be confirmed in a randomized, controlled clin. trial.

IT 111744-92-4, Hyalograft 3D

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(membrane; tissue engineering in treatment of diabetic foot ulcers)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 16 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:161838 CAPLUS

DOCUMENT NUMBER: 132:313587

TITLE: Hyaluronan-based **biopolymers** as delivery vehicles for bone-marrow-derived mesenchymal progenitors

AUTHOR(S): Radice, M.; Brun, P.; Cortivo, R.; Scapinelli, R.; Battaliard, C.; Abatangelo, G.

CORPORATE SOURCE: Institute of Histology and Embryology, University of Padova, Padua, I-35121, Italy

SOURCE: Journal of Biomedical Materials Research (2000), 50(2), 101-109

CODEN: JBMRBG; ISSN: 0021-9304

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The tolerability and safety of hyaluronan-based 3-dimensional scaffolds as a culture vehicle for mesenchymal progenitor cells was investigated in this pilot study. The proliferation patterns and extracellular matrix prodn. of rabbit and human mesenchymal, bone-marrow-derived progenitors first were characterized in vitro. Subsequently rabbit autologous cells were cultured in this hyaluronan-based scaffold and implanted in a full-thickness osteochondral lesion. In vitro histol. findings showed that mesenchymal progenitor cells adhered and proliferated onto the hyaluronan-derived scaffold. Human stem cells produced the main extracellular matrix mols., accompanied by an occasional synthesis of mature type II collagen. In vivo data demonstrated that the biomaterial, with or without mesenchymal progenitors, did not elicit any inflammatory response and was completely degraded within 4 mo after implantation. With regard to the efficacy of this cell therapy, even among the small no. of animals tested there was histol. evidence that lesions filled with the biomaterial, either seeded or unseeded with cells, achieved a faster and better healing compared to empty controls. The present data suggest that the hyaluronan-based scaffolds are well tolerated and safe and may be a valuable delivery vehicle for tissue engineering in the repair of articular cartilage defects.

IT 111744-92-4, Hyaff 11

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hyaluronan-based **biopolymers** as delivery vehicles for bone-marrow-derived mesenchymal progenitors)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 17 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:524997 CAPLUS

DOCUMENT NUMBER: 131:174985

TITLE: Effect of process parameters on the supercritical antisolvent precipitation of microspheres of **natural polymers**

AUTHOR(S): Reverchon, E.; De Rosa, I.; Della Porta, G.

CORPORATE SOURCE: Dipartimento Ingegneria Chimica Alimentare, Universita

SOURCE: Salerno, Fisciano, I-84084, Italy  
Wissenschaftliche Berichte - Forschungszentrum  
Karlsruhe (1999), FZKA 6271, High Pressure Chemical  
Engineering, 251-254  
CODEN: WBFKF5; ISSN: 0947-8620

DOCUMENT TYPE: Report

LANGUAGE: English

AB Several polysaccharides are currently used as drug delivery system in form of microspheres and various routes were used to prep. such microparticles. In this work, continuous supercrit. antisolvent pptn. (SAS) was used to produce sub-micronic particles of various natural polymers, such as inulin, dextran, and poly(hyaluronic acid) (HYAFF 11). Supercrit. CO2 as the supercrit. antisolvent and DMSO as the liq. solvent was used. The effect of pressure, temp., and liq. soln. concn. was studied on the morphol., particle size, and particle size distribution of polymer particles.

IT 111744-92-4, HYAFF 11  
RL: PEP (Physical, engineering or chemical process); PROC (Process)  
(effect of process parameters on supercrit. antisolvent pptn. of microspheres of **natural polymers**)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 18 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:811119 CAPLUS

DOCUMENT NUMBER: 132:40589

TITLE: **Three-dimensional** prostheses  
containing hyaluronic acid derivatives

INVENTOR(S): Pastorello, Andrea; Radice, Marco; Callegaro, Lanfranco

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.L., Italy

SOURCE: PCT Int. Appl., 24 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965534	A1	19991223	WO 1999-EP4167	19990616
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335023	AA	19991223	CA 1999-2335023	19990616
EP 1087797	A1	20010404	EP 1999-929241	19990616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002518101	T2	20020625	JP 2000-554411	19990616
AU 761325	B2	20030605	AU 1999-46115	19990616
US 6642213	B1	20031104	US 2000-719200	20001208
PRIORITY APPLN. INFO.:		IT 1998-PD149	A	19980617
		WO 1999-EP4167	W	19990616

AB A three-dimensional prosthesis is described in the shape of a body part comprising at least one three-dimensional matrix having an essentially fibrous or porous structure and contg. a hyaluronic acid deriv. The prosthesis contains at least two of the 3-dimensional matrixes, the first of the matrixes incorporating or being adhered to the second and possible

further matrixes, the matrix(es) optionally incorporating and/or being adhered to a bidimensional perforated matrix and contg. a hyaluronic acid deriv. This prosthesis is used for reconstruction of human or animal body part.

IT 111744-92-4, Benzyl hyaluronate

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(three-dimensional prostheses contg. hyaluronate

and cells and polymers for reconstruction of body parts)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 19 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:414463 CAPLUS

DOCUMENT NUMBER: 131:174989

TITLE: Chondrocyte aggregation and reorganization into three-dimensional scaffolds

AUTHOR(S): Brun, Paola; Abatangelo, Giovanni; Radice, Marco; Zacchi, Valentina; Guidolin, Diego; Gordini, Daniela Daga; Cortivo, Roberta

CORPORATE SOURCE: Institute of Histology and Embryology, Faculty of Medicine, University of Padova, Padua, I-35121, Italy

SOURCE: Journal of Biomedical Materials Research (1999), 46(3), 337-346

CODEN: JBMRBG; ISSN: 0021-9304

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Articular cartilage has a very limited self-repairing capacity; thus, chondral lesions normally result in chronic degeneration and, eventually, osteoarthritis development. Currently, tissue engineering offers a new tool for the clin. treatment of osteochondral defects. The present investigation aimed to develop an in vitro engineered cartilage using a new class of semisynthetic scaffolds. Two non-woven meshes of hyaluronan esters (Hyaff derivs.) were seeded with sternal chick embryo chondrocytes cultured for up to 21 days, after which time they were assessed for both the cellular growth profile and histol. features. Avian chondrocytes easily adhered and proliferated onto hyaluronan-based scaffolds, demonstrating a significant preference for the fully esterified benzylic form. Histochem. staining revealed the presence of a neo-synthesized glycosaminoglycan-rich extracellular matrix, and immunohistochem. confirmed the deposition of collagen type II. Moreover, ultrastructural observations supported evidence that chondrocytes grown onto a hyaluronan-derived three-dimensional scaffold maintained their unique phenotype and organization in a cartilage-like extracellular matrix. These findings support the further pursuit of a transplantable engineered cartilage using human chondrocytes for the regeneration of chondral lesions.

IT 111744-92-4, Hyaff 11

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(non-woven meshes; chondrocyte aggregation and reorganization into 3-dimensional scaffolds)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 20 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:568592 CAPLUS

DOCUMENT NUMBER: 132:15516

TITLE: Mechanisms controlling diffusion and release of model proteins through and from partially esterified hyaluronic acid membranes

AUTHOR(S): Simon, L. D.; Stella, V. J.; Charman, W. N.; Charman, S. A.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, KS, USA  
SOURCE: Journal of Controlled Release (1999), 61(3), 267-279  
CODEN: JCREEC; ISSN: 0168-3659  
PUBLISHER: Elsevier Science Ireland Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The effects of polymer percent esterification and protein mol. wt. on the diffusion of two model proteins, DNase (DNase) and RNase A (RNase A), through and from partially esterified hyaluronic acid membranes were compared. The permeability of the polymer membranes was inversely related to the degree of polymer esterification and the mol. wt. of the protein. Transport rates of proteins through the membranes decreased dramatically over narrow ranges of polymer esterification. As expected, the apparent diffusivity of the larger protein in the polymer matrix was more sensitive to changes in membrane hydration than that of the smaller protein. These observations demonstrated the dependence of the mobility of large mol. wt. proteins on polymer hydration and chain relaxation. The relationship between protein diffusion through and release from the modified hyaluronate matrixes was also investigated using RNase A as a model. The release profiles from fully esterified membranes showed lag behavior and varied with protein load and hyaluronate hydrolysis rates, while release from less esterified membranes was rapid and independent of polymer esterification or hydrolysis. Potential applications of modified hyaluronate matrixes in the controlled delivery of proteins are discussed.

IT 111744-92-4, Benzyl hyaluronate

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanisms controlling diffusion and release of model proteins through and from partially esterified hyaluronic acid membranes)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 21 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:290916 CAPLUS

DOCUMENT NUMBER: 131:106753

TITLE: Hyaluronic acid-based polymers as cell carriers for tissue-engineered repair of bone and cartilage

AUTHOR(S): Solchaga, Luis A.; Dennis, James E.; Goldberg, Victor M.; Caplan, Arnold I.

CORPORATE SOURCE: Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, OH, 44106-7080, USA

SOURCE: Journal of Orthopaedic Research (1999), 17(2), 205-213  
CODEN: JOREDR; ISSN: 0736-0266

PUBLISHER: Journal of Bone and Joint Surgery, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Culture-expanded bone marrow-derived mesenchymal progenitor cells differentiate into chondrocytes or osteoblasts when implanted s.c. in vivo in combination with an appropriate delivery vehicle. This in vivo implantation technique is used to test new materials as putative delivery vehicles in skeletal tissue-engineering models. HYAFF 11 and ACP sponges, 2 biomaterials based on hyaluronic acid modified by esterification of the carboxyl groups of the glucuronic acid, were tested as osteogenic or chondrogenic delivery vehicles for rabbit mesenchymal progenitor cells and compared with a well characterized porous calcium phosphate ceramic delivery vehicle. The implant materials were examd. by SEM for differences in pore structure or cellular interactions, were quantified for their ability to bind and retain mesenchymal progenitor cells, and were examd. histol. for their ability to support osteogenesis and chondrogenesis after s.c. implantation into nude mice. The ACP sponge bound the same no. of cells as fibronectin-coated ceramic, whereas the

HYAFF 11 sponge bound 90% more. When coated with fibronectin, ACP and HYAFF 11 bound, resp., 100 and 130% more cells than the coated ceramics. HYAFF 11 sponge composites retained their integrity after the 3 or 6-wk incubation period in the animals and were processed for histomorphometric anal. As a result of rapid degrdn. or resorption in vivo, ACP sponges could not be recovered after implantation and could not be analyzed. HYAFF 11 sponges presented more area available for cell attachment and more available vol. for newly formed tissue. Following loading with mesenchymal progenitor cells and implantation, the pores of the sponges contained more bone and cartilage than the pores of ceramic cubes at either time point. Thus, relative to ceramic, HYAFF 11 sponges allow incorporation of twice as many cells and produce a 30% increase in the relative amt. of bone and cartilage/unit area. Hence, the hyaluronic acid-based delivery vehicles are superior to porous calcium phosphate ceramic with respect to the no. of cells loaded per unit vol. of implant, and HYAFF 11 sponges are superior to the ceramics with regard to the amt. of bone and cartilage formed. Addnl., hyaluronic acid-based vehicles have the advantage of degrdn./resorption characteristics that allow complete replacement of the implant with newly formed tissue.

IT 111744-92-4, Hyaff 11

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hyaluronic acid-based polymers as cell carriers for tissue-engineered repair of bone and cartilage)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 22 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:557802 CAPLUS

DOCUMENT NUMBER: 131:355969

TITLE: Variation in the diffusion and release of ribonuclease through and from esterified hyaluronic acid membranes: Effect of changes in matrix characteristics

AUTHOR(S): Simon, L. D.; Stella, V. J.; Charman, W. N.; Charman, S. A.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, KS, USA

SOURCE: Journal of Controlled Release (1999), 61(1-2), 159-164  
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Investigations were conducted using membranes composed of esterified hyaluronic acid to det. the effect of the phys. matrix properties on protein diffusion and release. Hyaluronate membranes prepd. by a solvent evapn. method formed 2 visually distinct regions, one transparent and the other translucent. Each of the 2 regions were characterized by DSC, FTIR, and Karl Fisher titrn. for water content. The transparent region exhibited a higher endothermic transition temp. and lower water content than obsd. for the translucent region. For the transparent region, significant lag times (>50 h) were detected for the transport and release of a model protein (RNase A) compared with that for the translucent region which showed no lag time. The results highlight the importance of carefully controlling matrix formation to ensure reproducible transport and release characteristics from polymer matrixes.

IT 111744-92-4, Benzyl hyaluronate

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(changes in matrix characteristics effect on variation in diffusion and release of RNase through and from esterified hyaluronic acid membranes)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 23 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:689257 CAPLUS  
DOCUMENT NUMBER: 129:261972  
TITLE: Dried contamination-free hydrocolloids and hydrogels of polysaccharides  
INVENTOR(S): Meister, Frank; Hueckel, Marion; Mueller, Peter-Juergen; Buehler, Konrad; Taplick, Thomas  
PATENT ASSIGNEE(S): Thueringisches Institut fuer Textil- und Kunststoff-Forschung e.V., Germany; Hans Knoell Institut fuer Naturstoff-Forschung e.V.; GWE Gesellschaft fuer Wissenschaft und Entwicklung m.b.H.  
SOURCE: Ger. Offen., 6 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19712708	A1	19981001	DE 1997-19712708	19970326

PRIORITY APPLN. INFO.: DE 1997-19712708 19970326  
AB Hydrocolloids and hydrogels of polysaccharides are dried with microwaves and optionally, simultaneously with IR and hot gas give products with low contamination, useful in pharmacy, cosmetics, medical technol., and biotechnol.  
IT 111744-92-4, Benzyl hyaluronate  
RL: PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); PROC (Process); USES (Uses)  
(microwave-dried contamination-free hydrocolloids and hydrogels of polysaccharides)  
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L126 ANSWER 24 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1997:450142 CAPLUS  
DOCUMENT NUMBER: 127:62875  
TITLE: Culture of bone marrow stem cells partially or completely differentiated into connective tissue cells in a three-dimensional biocompatible and biodegradable matrix of hyaluronic acid derivative  
INVENTOR(S): Abatangelo, Giovanni; Callegaro, Lanfranco  
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.R.L., Italy; Abatangelo, Giovanni; Callegaro, Lanfranco  
SOURCE: PCT Int. Appl., 34 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718842	A1	19970529	WO 1996-EP5093	19961119
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2238011	AA	19970529	CA 1996-2238011	19961119
AU 9676934	A1	19970611	AU 1996-76934	19961119
AU 709236	B2	19990826		

EP 863776 A1 19980916 EP 1996-939845 19961119  
 EP 863776 B1 20030129  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, FI, RO  
 JP 2000500372 T2 20000118 JP 1997-519385 19961119  
 AT 231730 E 20030215 AT 1996-939845 19961119  
 ES 2189890 T3 20030716 ES 1996-939845 19961119  
 US 6596274 B1 20030722 US 1998-41287 19980312  
 US 6482231 B1 20021119 US 2000-602033 20000623

## PRIORITY APPLN. INFO.:

IT 1995-PD225 A 19951120  
 WO 1996-EP5093 W 19961119  
 US 1998-41287 A2 19980312  
 US 1998-39200 B1 19980313

AB A biol. material useful in skin grafts consists of (A) an efficient culture of autologous or homologous bone marrow stem cells partially or completely differentiated into connective tissue-specific cells, and the extracellular matrix secreted by these cells (or alternatively the extracellular matrix secreted by bone marrow stem cells partially or completely differentiated into a specific connective tissue or by the specific homologous mature connective tissue cells, said extracellular matrix being free from any cellular component) and (B) a 3-dimensional biocompatible and biodegradable matrix consisting of a hyaluronic acid deriv. Matrix (B) is free of immunogenic nonautologous proteins which might cause an immunol. reaction against the graft. Thus, a 3-dimensional nonwoven matrix of Hyaff 11 (benzyl hyaluronate) was seeded with human fibroblasts obtained from cultures of bone marrow mesenchymal stem cells and incubated in culture medium for 7-21 days to produce an artificial dermis. During incubation, the fibroblasts deposited an extracellular matrix contg. collagen types I, III, and IV, fibronectin, and laminin.

IT **111744-92-4, Benzyl** hyaluronate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (culture of bone marrow stem cells differentiated into connective tissue cells in three-dimensional biocompatible and biodegradable matrix of hyaluronic acid deriv.)

L126 ANSWER 25 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:609912 CAPLUS

DOCUMENT NUMBER: 125:230888

TITLE: Process for the coating of objects with hyaluronic acid, their derivatives, and **semisynthetic polymers**

INVENTOR(S): Morra, Marco; Cassinelli, Clara; Benedetti, Luca; Callegaro, Lanfranco

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers, S.R.L., Italy

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9624392	A1	19960815	WO 1996-EP509	19960207
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE			
CA 2212519	AA	19960815	CA 1996-2212519	19960207
AU 9647884	A1	19960827	AU 1996-47884	19960207
AU 704047	B2	19990415		



EP 808181	A1	19971126	EP 1996-904009	19960207
EP 808181	B1	20020619		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
BR 9607516	A	19971230	BR 1996-7516	19960207
CN 1173824	A	19980218	CN 1996-191809	19960207
JP 10513378	T2	19981222	JP 1996-523988	19960207
HU 219815	B	20010828	HU 1997-2114	19960207
RU 2173563	C2	20010920	RU 1997-115374	19960207
PL 182804	B1	20020329	PL 1996-321781	19960207
AT 219381	E	20020715	AT 1996-904009	19960207
ES 2179930	T3	20030201	ES 1996-904009	19960207
NO 9703648	A	19971003	NO 1997-3648	19970807
US 6129956	A	20001010	US 1997-930858	19971007

## PRIORITY APPLN. INFO.:

IT 1995-PD30	A	19950207
IT 1995-PD243	A	19951220
WO 1996-EP509	W	19960207

AB Processes are provided for coating the surfaces of objects with hyaluronic acid, its derivs. or other natural or semisynthetic polymers, for applications in the fields of surgery, health care and diagnostics. The processes make it possible to bind such polymers in a stable manner to the surfaces of objects made of a wide range of materials. Surfaces treated according to the processes are characterized by a high degree of wettability, and are able to inhibit the adhesion of celles or bacteria present in the biol. fluids.

IT **111744-92-4, Benzyl** hyaluronate

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(coating of objects with hyaluronic acid, derivs., and  
**semisynthetic polymers**)

L126 ANSWER 26 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:915953 CAPLUS

DOCUMENT NUMBER: 123:315553

TITLE: Blends of **synthetic** and **natural polymers** as special performance materials

AUTHOR(S): Giusti, Paolo; Lazzeri, Luigi; Cascone, Maria Grazia; Seggiani, Maurizia

CORPORATE SOURCE: Dipartimento di Ingegneria Chimica, Universita di Pisa, Pisa, Italy

SOURCE: Macromolecular Symposia (1995), 100(5th European Polymer Federation Symposium on Polymeric Materials, 1994), 81-7

CODEN: MSYMEC; ISSN: 1022-1360

PUBLISHER: Huethig & Wepf

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The prepn. and characterization of blends of hyaluronic acid (or its benzyl ester) and poly(vinyl alc.) (or ethylene-vinyl alc. copolymers) were reported.

IT **111744-92-4, Hyaluronic acid, benzyl** ester

RL: PRP (Properties)  
(blends of **synthetic** and **natural polymers**  
as special performance materials)

L126 ANSWER 27 OF 55 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:414293 CAPLUS

DOCUMENT NUMBER: 117:14293

TITLE: Methylprednisolone esters of hyaluronic acid in ophthalmic drug delivery: in vitro and in **vivo** release studies

AUTHOR(S): Kyyronen, Kristiina; Hume, Lisbeth; Benedetti, Luca; Urtti, Arto; Topp, Elizabeth; Stella, Valentino

CORPORATE SOURCE: Dep. Pharm. Chem., Univ. Kansas, Lawrence, KS,

SOURCE: 66045-2504, USA  
International Journal of Pharmaceutics (1992),  
80(2-3), 161-9  
CODEN: IJPHDE; ISSN: 0378-5173

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Films and microspheres were prepd. from various esters of hyaluronic acid. A model drug, methylprednisolone, was either phys. incorporated into the polymer matrix or chem. bound to the polymer backbone through an ester linkage. In vitro release from films with covalently bound drug was much slower (t50% = 71 h) than that for phys. dispersed drug (t50% = 2.5-17 h). Methylprednisolone concns. in the tear fluid of New Zealand rabbits were measured after ocular application of drug (approx. 420 .mu.g) in different dosage forms. When methylprednisolone was phys. dispersed in the polymer matrix, in vivo drug release from matrixes was slower than that obsd. in vitro. Compared with a suspension control, peak methylprednisolone concns. in tear fluid were 9-14 times lower after administration of drug in polymer films and AUC0-8h values were 4-7 times higher. These results imply that hyaluronic acid ester preps. can increase the residence time of methylprednisolone in the tear fluid of rabbits.

IT 111744-92-4, **Benzyl** hyaluronate  
RL: BIOL (Biological study)  
(films and microspheres, for methylprednisolone eye delivery)

L126 ANSWER 28 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 1

ACCESSION NUMBER: 2003497423 EMBASE

TITLE: Clinical aspects and strategy for biomaterial engineering of an auricle based on three-dimensional stereolithography.

AUTHOR: Naumann A.; Aigner J.; Staudenmaier R.; Seemann M.; Bruening R.; Englmeier K.H.; Kadegge G.; Pavesio A.; Kastenbauer E.; Berghaus A.

CORPORATE SOURCE: A. Naumann, Dept. Otorhinolaryngology Hd. N., Ludwig Maximilian University, Marchioninstr. 15, 81377 Munich, Germany. andreas.naumann@hno.med.uni-muenchen.de

SOURCE: European Archives of Oto-Rhino-Laryngology, (2003) 260/10 (568-575).  
Refs: 50  
ISSN: 0937-4477 CODEN: EAOTE7

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 009 Surgery  
011 Otorhinolaryngology  
027 Biophysics, Bioengineering and Medical Instrumentation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB At the present time, the partial and/or complete reconstruction of an auricle from autologous rib cartilage is one of most widely published techniques. In the field of tissue engineering, different techniques have been described to generate cartilage tissue using isolated chondrocytes. The basis of these tissue-engineering techniques is bioresorbable or non-bioresorbable biomaterials, which serve as a three-dimensional cell carrier. Tissue engineering of an auricle requires preformed bioresorbable biomaterials designed to fit the form of a patient's auricular defect. Three-dimensional imaging acquired from computed tomography scans or laser surface scanning has become an important tool in modern medicine. This study represents the preoperative procedures for the reconstruction of an auricle through tissue engineering in accordance with the clinical aspects. Hyaff 11, a hyaluronic acid derivative, was used as a

three-dimensional cell carrier for isolated human nasoseptal chondrocytes. The chondrocytes were amplified in a conventional monolayer culture before the cells were seeded on a hyaluronic non-woven mesh and cultured in vitro for 4 weeks. The chondrogenic potential of human nasal chondrocytes in Hyaff 11 was investigated by confocal laser scanning microscopy, histology (toluidine blue) and immunohistochemistry (collagen type II). Computer-aided design (CAD) and manufacture of an auricle model with stereolithographical methods were used for the prefabrication of a bioresorbable three-dimensional cell carrier designed in the form of a patient's auricular defect. The cell carrier used was Hyaff 11, a fully **benzyl**-esterified hyaluronic acid derivative. Confocal laser scanning microscopy has shown good cell attachment, a homogenous distribution of amplified chondrocytes and a viability of more than 90%. After 4 weeks in vitro culture the human nasoseptal chondrocytes synthesized new cartilage with the expression of cartilage-specific collagen type II. In order to shape a patient's designed scaffold the auricle model was fitted exactly and symmetrically to the contralateral side. Subsequently, the mirror image patient-specific model was used to prepare an identical scaffold model made of a fully **benzyl**-esterified hyaluronic acid derivative. The bioresorbable scaffold that was produced gave a satisfactory representation of auricle structure. Bioresorbable preformed biomaterials in the form of a patient's auricle defect represent an important prerequisite for the tissue engineering of autologous auricle grafts. Hyaff 11 seems to be a promising material for tissue engineering of cartilage transplants, and the application of this approach will improve conventional reconstructive surgery in the future.

L126 ANSWER 29 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3

ACCESSION NUMBER: 2001047051 EMBASE  
TITLE: Morphology and metabolism of hepatocytes cultured in Petri dishes on films and in non-woven fabrics of hyaluronic acid esters.  
AUTHOR: Catapano G.; De Bartolo L.; Vico V.; Ambrosio L.  
CORPORATE SOURCE: G. Catapano, Department Chemical/Materials Eng., University of Calabria, Via P. Bucci cubo 17/C, I-87030 Rence (CS), Italy. catapano@unical.it  
SOURCE: Biomaterials, (2001) 22/7 (659-665).  
Refs: 28  
ISSN: 0142-9612 CODEN: BIMADU  
PUBLISHER IDENT.: S 0142-9612(00)00228-3  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology  
002 Physiology  
027 Biophysics, Bioengineering and Medical Instrumentation  
029 Clinical Biochemistry  
048 Gastroenterology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Polymers of hyaluronic acid (Hyal) esters exhibit good tissue compatibility and are available in various geometrical configurations. These properties can be exploited for the design of innovative bioartificial liver support devices (BALSDs) using primary hepatocytes. In this paper, we report a preliminary investigation of the polymer feasibility of the ethyl and the benzyl Hyal ester in the form of films and non-woven fabrics for the in vitro culture of primary rat hepatocytes. Cell function was evaluated daily in Petri dishes with respect to the rate of ammonia elimination (AER) and urea synthesis (USR). Cells cultured in non-woven fabrics of the ethyl ester of Hyal (HYAFF7(nw)) exhibited an initial AER about 32% lower and synthesised urea 33% faster than that of cells on collagen films. After a week in culture, cells on collagen films

retained only a minor fraction of their initial rates. Cells cultured in non-woven fabrics of HYAFF7(nw) retained about 62 and 44% of their initial AER and USR, respectively, and exhibited an AER approximately equal to and a USR 3.6 times greater than those of cells adherent to collagen. These results suggest that non-woven fabrics of HYAFF7(nw) are promising substrata for hepatocyte culture in BALSDs. Copyright .COPYRGT. 2001 Elsevier Science Ltd.

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on STN DUPLICATE 5

ACCESSION NUMBER: 1999414118 EMBASE  
TITLE: In vitro reconstructed tissues on hyaluronan-based temporary scaffolding.  
AUTHOR: Brun P.; Cortivo R.; Zavan B.; Vecchiato N.; Abatangelo G.  
CORPORATE SOURCE: G. Abatangelo, Institute Histology and Embryology, Faculty of Medicine, University of Padova, Viale G. Colombo 3, 35121 I-Padova, Italy. abatange@civ.bio.unipd.it  
SOURCE: Journal of Materials Science: Materials in Medicine, (1999) 10/10-11 (683-688).  
Refs: 62  
ISSN: 0957-4530 CODEN: JSMMEI  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology  
013 Dermatology and Venereology  
027 Biophysics, Bioengineering and Medical Instrumentation  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Tissue engineering offers the possibility to reconstruct tissue substitutes in order to replace lost or damaged tissues. The availability of appropriate biomaterial devices is essential to allow in vitro cultured cells to behave as in the original tissues in vivo. In our studies we utilized a seminatural biomaterial made up by the **benzyl** ester of hyaluronan to grow keratinocytes, fibroblasts and chondrocytes. Keratinocytes and fibroblasts were isolated from human foreskin. Cells were separately cultured on two different hyaluronan based biomaterial devices for the first 15 days and then co-cultured for an additional period of 2 weeks. Keratinocytes gave rise to a well-differentiated epithelial layer, while fibroblasts were able to synthesize all the main extracellular molecules inside the biomaterial spaces, forming dermal-like tissues. When these two tissues were co-cultured, a skin equivalent was formed with a dermal-epidermal junction. Chondrocytes were obtained from chick-embryo sterna and cultured for 21 days inside a non-woven scaffolding made up of a hyaluronan-based biomaterial. Cells were able to organize themselves into nodules embedded in a dense metachromatic substance in which type II collagen was present. Data from this study suggest that this novel class of hyaluronan derived biomaterials is suitable for different cell culture and in vitro tissue reconstruction.

L126 ANSWER 31 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 2002103474 EMBASE  
TITLE: Comparison of the antioxidant properties of HYAFF.RTM.-11p75, AQUACEL.RTM. and hyaluronan towards reactive oxygen species in vitro.  
AUTHOR: Moseley R.; Leaver M.; Walker M.; Waddington R.J.; Parsons D.; Chen W.Y.J.; Embery G.  
CORPORATE SOURCE: R. Moseley, Department of Basic Dental Science, Dental School, Univ. of Wales College of Medicine, Heath Park, Cardiff, Wales CF14 4XY, United Kingdom.  
Moseleyr@cardiff.ac.uk  
SOURCE: Biomaterials, (2002) 23/10 (2255-2264).

Refs: 49  
ISSN: 0142-9612 CODEN: BIMADU  
PUBLISHER IDENT.: S 0142-9612(01)00360-X  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 013 Dermatology and Venereology  
027 Biophysics, Bioengineering and Medical  
Instrumentation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In chronic wounds, a number of host factors are released which perpetuate the inflammatory process, including polymorphonuclear leukocyte (PMN)-derived reactive oxygen species (ROS), such as superoxide radical ( $O(2)(\cdot)$ ) and hydroxyl radical ( $(\cdot)OH$ ) species. The glycosaminoglycan, hyaluronan, has been shown to act as an antioxidant towards ROS, although the potential for biomaterials, such as HYAFF.RTM.-11p75 (the 75% benzyl ester of hyaluronan) and AQUACEL.RTM. (carboxymethylcellulose), to act in this manner has yet to be elucidated. This study compared the antioxidant properties of high and low molecular weight hyaluronan (HMWT HA and LMWT HA), HYAFF.RTM.-11p75, AQUACEL.RTM. and an AQUACEL.RTM./hyaluronan composite (AQUACEL.RTM./HA) against  $O(2)(\cdot)$  and  $(\cdot)OH$ . The antioxidant capacities of each material were assessed by their ability to inhibit cytochrome C reduction by  $O(2)(\cdot)$  fluxes, generated via the oxidation of hypoxanthine by xanthine oxidase, and their inhibition of 2-deoxy-D-ribose degradation by  $(\cdot)OH$  fluxes, generated by the reaction of hydrogen peroxide ( $H(2)O(2)$ ) and iron ( $Fe(2+)$ ). All materials studied possessed dose dependent antioxidant properties towards  $O(2)(\cdot)$ , with HYAFF.RTM.-11p75 having the greatest antioxidant potential towards these species, followed by AQUACEL.RTM., HMWT HA, AQUACEL.RTM./HA and LMWT HA. Only HMWT HA exhibited dose dependent antioxidant properties towards  $(\cdot)OH$  at the fluxes examined. Gas chromatography/mass spectrometry analysis implied that ester bonds between the hyaluronan backbone and benzyl groups of HYAFF.RTM.-11p75 are highly susceptible to  $O(2)(\cdot)$  hydrolysis, with the de-esterified benzyl alcohol being rapidly degraded in the presence of  $(\cdot)OH$ . This data supports the hypothesis that HYAFF.RTM.-11p75 has greater antioxidant capacity towards  $O(2)(\cdot)$ , due to the esterified benzyl groups providing alternative sites for  $O(2)(\cdot)$  attack other than the hyaluronan backbone of HYAFF.RTM.-11p75 itself and explains the inability of HYAFF.RTM.-11p75 to scavenge  $(\cdot)OH$ , due to benzyl alcohol degradation by  $(\cdot)OH$ . The antioxidant activities of these biomaterials, particularly HYAFF.RTM.-11p75 and AQUACEL.RTM., towards  $O(2)(\cdot)$  could be beneficial, as the scavenging of PMN-derived  $O(2)(\cdot)$  may remove initial sources of  $O(2)(\cdot)$  and further prevent the secondary formation of  $(\cdot)OH$ . These ROS are thought to be a primary causal factor for the extensive degradation and metabolic alterations observed in chronic wounds. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.

L126 ANSWER 32 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2002296709 EMBASE  
TITLE: New microencapsulated sunscreens: Technology and comparative evaluation.  
AUTHOR: Anselmi C.; Centini M.; Rossi C.; Ricci M.; Rastrelli A.; Andreassi M.; Buonocore A.; La Rosa C.  
CORPORATE SOURCE: C. Anselmi, Dipto. Farmaco Chimico Tecnologico, Sc. di Spec. in Sci. e Tecn. Cosmet., Universita di Siena, Via della Diana 2, 53100 Siena, Italy. anselmic@unisi.it  
SOURCE: International Journal of Pharmaceutics, (21 Aug 2002) 242/1-2 (207-211).  
Refs: 12

ISSN: 0378-5173 CODEN: IJPHDE  
PUBLISHER IDENT.: S 0378-5173(02)00159-X  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The aim of this work is to obtain new technologically improved microencapsulated sunscreens characterised by UV-radiation stability, good substantivity, low toxicity, a better tolerability and easiness to formulation. For this purpose we prepared two different systems using semisynthetic Hyaluronic Acid (HA) benzyl ester and a synthetic polymer (patent pending). We obtained these systems using two different methodologies: emulsification/solvent evaporation and emulsification/solvent extraction. The comparison between the two formulated systems was carried out in terms of their chemical-physical and biological properties. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L126 ANSWER 33 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 96160646 EMBASE  
DOCUMENT NUMBER: 1996160646  
TITLE: Quantitative assessment of the tissue response to films of hyaluronan derivatives.  
AUTHOR: Campoccia D.; Hunt J.A.; Doherty P.J.; Zhong S.P.; O'Regan M.; Benedetti L.; Williams D.F.  
CORPORATE SOURCE: Department of Clinical Engineering, University of Liverpool, PO Box 147, Liverpool L69 3BX, United Kingdom  
SOURCE: Biomaterials, (1996) 17/10 (963-975).  
ISSN: 0142-9612 CODEN: BIMADU  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The aim of this study was to evaluate the in vivo response following implantation into a rat model of three innovative hyaluronan derivatives for clinical use: HYAFF 7, HYAFF 11 and HYAFF 11p75 (respectively, the 100% ethyl ester, 100% and 75% **benzyl** esters). The tissue reaction evoked by films of these new biomaterials implanted into the dorsolumbar musculature of rats was assessed quantitatively using a well established technique based upon an image analysis system. The number of inflammatory cells present and the patterns of cell distribution around the implant up to a distance of 642 .mu.m were examined at different time periods after implantation. Since a well-delineated tissue-material interface was needed for this type of investigation, it was not possible to apply image analysis to sections once dissolution of the implanted materials had begun. Films of both the total esters, HYAFF 7 and HYAFF 11, were found to undergo a slow dissolution process and, after a month, films of these materials were still present at the site of implantation. Differences in response to the two materials were observed only during the first two weeks, particularly with respect to neutrophil distribution and total cellularity. HYAFF 7 was found to be more reactive, with higher numbers of neutrophils near the surface of the implant than HYAFF 11. Thereafter, the differences between the two materials were minimal and owing mainly to a faster dissolution of HYAFF 7 films. After 3 and 5 months, considerable degradation of films of both total esters had occurred. Significant quantities of material appeared inside numerous macrophages with an ED1-positive phenotype. Only a very thin layer of fibrous connective tissue, indicative of low reactivity, was found to

surround the site of implantation, separating the dissolved material and the phagocytic cells from healthy muscular tissue. ED2-positive macrophages were primarily confined within the lining connective tissue. The partial **benzyl** ester, HYAFF 11p75, showed a different behaviour. In fact, evidence of film dissolution was already present a week after the implantation. After two weeks, the implanted films were completely dissolved and numerous ED1-positive macrophages phagocytosing the material were observed at the site of implantation. Therefore, in agreement with previous in vitro studies, which showed a greater susceptibility to degradation of hyaluronan derivatives with lower percentage of esterification, HYAFF 11p75 underwent resorption faster than the corresponding total ester.

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on STN

ACCESSION NUMBER: 95274627 EMBASE  
DOCUMENT NUMBER: 1995274627  
TITLE: Solute diffusion in ionizable hydrogels.  
AUTHOR: Topp E.M.; Sung K.C.  
CORPORATE SOURCE: Dept. Pharmaceutical Chemistry, University of  
Kansas, Lawrence, KS 66045, United States  
SOURCE: Proceedings of the Controlled Release Society, (1995) -/22  
(348-349).  
ISSN: 1022-0178 CODEN: 58GMAH  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical  
Instrumentation  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English

L126 ANSWER 35 OF 55 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 94290652 EMBASE  
DOCUMENT NUMBER: 1994290652  
TITLE: Ocular sustained delivery of prednisolone using hyaluronic  
acid benzyl ester films.  
AUTHOR: Hume L.R.; Lee H.K.; Benedetti L.; Sanzgiri Y.D.; Topp  
E.M.; Stella V.J.  
CORPORATE SOURCE: Dept. of Pharmaceutical Chemistry, Center for Drug Delivery  
Research, University of Kansas, Lawrence, KS 66045-2504,  
United States  
SOURCE: International Journal of Pharmaceutics, (1994) 111/3  
(295-298).  
ISSN: 0378-5173 CODEN: IJPHDE  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 012 Ophthalmology  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Hyaluronic acid benzyl ester films were studied for ocular delivery of prednisolone. The four polymers used were HYAFF 11 p25 (25% benzyl ester, 75% sodium salt), HYAFF 11 p50 (50% benzyl ester, 50% sodium salt), HYAFF 11 p75 (75% benzyl ester, 25% sodium salt) and HYAFF 11 (100% benzyl ester). The polymer with the lowest degree of esterification, HYAFF 11 p25, was the most hydrophilic and released drug faster than those with higher degrees of esterification, HYAFF 11 and HYAFF 11 p75, which are generally less hydrophilic. Tear fluid prednisolone concentrations were measured in rabbits after administration of the test films. Areas under the tear fluid concentration vs time curves (AUC(0-8 h)) were calculated

for all the dosage forms, from the time of dosing to 8 h post-dosing. The HYAFF 11 p25 films provided higher initial concentrations which rapidly declined below 30  $\mu\text{g/ml}$ , 2 h post-dosing. Concentrations for the HYAFF 11 p75 film dropped below 30  $\mu\text{g/ml}$ , 3 h post-dosing. The HYAFF 11 films provided the best results with sustained concentrations between 45 and 72  $\mu\text{g/ml}$  for the 8 h study period. The results show that sustained delivery of prednisolone to the eye may be achieved with the use of hyaluronic acid esters.

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on STN

ACCESSION NUMBER: 92182077 EMBASE  
DOCUMENT NUMBER: 1992182077  
TITLE: Drug release from membranes of hyaluronic acid and its esters.  
AUTHOR: Joshi H.N.; Stella V.J.; Topp E.M.  
CORPORATE SOURCE: Department Pharmaceutical Chemistry, University of Kansas, Lawrence, KS 66045-2504, United States  
SOURCE: Journal of Controlled Release, (1992) 20/2 (109-121).  
ISSN: 0168-3659 CODEN: JCREEC  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Drug release from three types of hyaluronated based (sodium hyaluronate and ethyl and benzyl esters of hyaluronic acid) membranes was investigated. In the membranes, drug was either: 1) physically incorporated, 2) physically incorporated in the membrane, then laminated with a second polymer or 3) covalently bound to the polymer. The release of model compounds was found to be rapid when the compounds were physically incorporated; the release could be slowed by laminating the core membranes. Permeability and partition coefficient values were used to explain the release profiles. The amount of drug released was linearly related to the square root of time for both 'physically incorporated' and 'laminated' systems. When drug was covalently bound to the polymer, the release was slow and near zero-order. The solubility of the polymer and/or the hydrolysis of ester bonds are thought to be some of the important processes involved in drug release. The results suggest that a range of release rates can be achieved with hyaluronate based membrane systems.

L126 ANSWER 37 OF 55 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1996-06698 DRUGU G  
TITLE: Effect of drug hydrophilicity and membrane hydration on diffusion in hyaluronic acid ester membranes.  
AUTHOR: Sung K C; Topp E M  
CORPORATE SOURCE: Univ.Kansas  
LOCATION: Lawrence, Kans., USA  
SOURCE: J.Controlled Release (37, No. 1-2, 95-104, 1995) 4 Fig. 2  
Tab. 18 Ref.  
CODEN: JCREEC ISSN: 0168-3659  
AVAIL. OF DOC.: Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS 66045-2504, U.S.A. (E.M.T.).  
LANGUAGE: English  
DOCUMENT TYPE: Journal  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature  
AB The permeation of hydrophilic drugs (5-fluorouracil (5-FU) theophylline (TH), and thymidine (TY) (all Sigma-Chem.)) through hydrated membranes



prepared from partial **benzyl esters** of **hyaluronic acid** (HA: HYAFF, Fidia) was consistent with free volume theory (i.e. via fluctuating **pores** or channels within the polymer matrix). Deviations from free volume theory were found for hydrophobic drugs (propylparaben (PP), fluocinolone acetonide (FA) and hydrocortisone (HC) (all Sigma-Chem.)) suggesting that interaction with the polymer and diffusion through polymer-rich domains contributed to their cumulative permeation behavior.

L126 ANSWER 38 OF 55 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 1998-0490292 PASCAL  
COPYRIGHT NOTICE: Copyright .COPYRG. 1998 INIST-CNRS. All rights reserved.  
TITLE (IN ENGLISH): Cartilage tissue engineering with novel **nonwoven** structured biomaterial based on **hyaluronic acid benzyl ester**  
AUTHOR: AIGNER J.; TEGELER J.; HUTZLER P.; CAMPOCCIA D.; PAVESIO A.; HAMMER C.; KASTENBAUER E.; NAUMANN A.  
CORPORATE SOURCE: Department of Otorhinolaryngology, Ludwig-Maximilians University of Munich, Germany, Federal Republic of; Department of Pathology, GSF Neuherberg, Oberschleissheim, Germany, Federal Republic of; Fidia Advanced Biopolymers Srl, Abano Terme, Italy; Institute of Surgical Research, Ludwig-Maximilians University of Munich, Germany, Federal Republic of  
SOURCE: Journal of biomedical materials research, (1998), 42(2), 172-181, 48 refs.  
ISSN: 0021-9304 CODEN: JBMRBG  
DOCUMENT TYPE: Journal  
BIBLIOGRAPHIC LEVEL: Analytic  
COUNTRY: United States  
LANGUAGE: English  
AVAILABILITY: INIST-13764, 354000070366930020

AB The aim of this study was to investigate the possibility of using the **benzyl ester** of **hyaluronic acid** (HYAFF.RTM. 11), a recently developed semisynthetic resorbable material, as a scaffold for the culture of human nasoseptal chondrocytes in tissue-engineering procedures of cartilage reconstruction. Different techniques such as immunohistochemistry, scanning electron microscopy, and confocal laser scanning microscopy were used to study the behavior, morphology, and phenotype expression of the chondrocytes, which were initially expanded and then seeded on the material. The **nonwoven** cell carrier allowed good viability and adhesivity of the cells without any surface treatment with additional substances. Furthermore, the cultured cells expressed cartilage-specific collagen type II, indicating that they were able to redifferentiate within the scaffold of HYAFF.RTM. 11 and were able to retain a chondrocyte phenotype even after a long period of in vitro conditions. Nevertheless, the expression of collagen type I, which was produced by dedifferentiated or incompletely redifferentiated chondrocytes, was noticeable. Additional data were obtained by subcutaneous implantation of samples seeded with human cells in the in vivo model of the athymic nude mouse. The results after 1 month revealed the development of tissue similar to hyaline cartilage. This study is promising for the use of this scaffold for tissue engineering of cartilage replacements.

L126 ANSWER 39 OF 55 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 2002:34251070 BIOTECHNO  
TITLE: Platelet adhesion to commercial and modified polymer materials in animals under psychological stress and in a no-stress condition  
AUTHOR: Barbucci R.; Lamponi S.; Aloisi A.M.

CORPORATE SOURCE: R. Barbucci, Department of Chemical Technologies, Via  
Ettore Bastianini, 12, 53100 Siena, Italy.  
E-mail: barbucci@unisi.it

SOURCE: Biomaterials, (2002), 23/9 (1967-1973), 32  
reference(s)  
CODEN: BIMADU ISSN: 0142-9612

PUBLISHER ITEM IDENT.: S0142961201003234

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

AB It is well known that stressful stimuli change blood functions and that protein and platelet parameters are altered in humans and animals subjected to stress. We have examined the influence of psychological stress on the morphological responses of platelets on commercially available materials [polyester (VP), fluoropassivated polyester (VPF), **non-woven benzylic ester of hyaluronic acid** (Hyaff11)] and on materials synthesised (PUPA) and/or surface modified by sulphation (Hyaff11S) or by immobilisation of the anticoagulant molecules heparin and sulphated hyaluronic acid (PUPA-Heparin, PUPA-Hyals, Hyals-PET). Moreover, the anticoagulant activity (i.e. thrombin inactivation) of the materials was analysed. In the no-stress condition, the surfaces with a low degree of platelet adhesion were Hyaff11S, Hyals-PET, PUPA-Heparin and PUPA-Hyals. Hyaff11, PET and PUPA had the highest number of adherent platelets within the series. VP and VPF exhibited an intermediate behaviour. The exposure of animals to stress induced a dramatic change in platelet number and morphology on PET, Hyals-PET, PUPA, PUPA-Hyals and Hyaff11: there was a higher degree of platelet adhesion, increased platelet spreading and the appearance of pseudopodia. In VP, VPF, Hyaff11S and PUPA-Heparin, there were no changes in platelet adhesion in stress conditions with respect to the no-stress condition; the latter two materials, the only ones able to prolong thrombin time, had a very low number of adherent platelets.  
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L126 ANSWER 40 OF 55 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2002:33109037 BIOTECHNO

TITLE: Physico-chemical properties and degradability of  
**non-woven hyaluronan benzylic esters** as tissue  
engineering scaffolds

AUTHOR: Milella E.; Brescia E.; Massaro C.; Ramires P.A.;  
Miglietta M.R.; Fiori V.; Aversa P.

CORPORATE SOURCE: E. Milella, Interdisciplinary Research Center,  
University of Naples Federico II, P.le Tecchio 80,  
80125 Naples, Italy.  
E-mail: milella@unina.it

SOURCE: Biomaterials, (15 FEB 2002), 23/4 (1053-1063), 14  
reference(s)  
CODEN: BIMADU ISSN: 0142-9612

PUBLISHER ITEM IDENT.: S0142961201002174

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The development of biocompatible materials which can be processed into three-dimensional scaffolds and the design of appropriate configurations in order to enable the cellular infiltration and proliferation is a major issue in the tissue engineering. The **hyaluronan total benzyl ester** (Hyaff.RTM.11) has been found to be suitable substrate to grow a variety of cell types. Since structural, physical, chemical and biological data can help for tailoring appropriate scaffold for tissue engineering, information on chemico-physical

properties on degradability of **hyaluronan total benzyl ester non-woven** has been obtained. The thermal analysis, the evaluation of the surface chemical composition, the morphology, the mechanical behaviour and the swelling tests were carried out on these materials. The **hyaluronan total benzyl ester non-woven** showed a thermal stability up to 220.degree.C and the surface composition differed from that of the bulk for C-O and C-C contribution. No contaminant were detected. The **non-woven** swelled in culture medium. Moreover the mechanical tests showed that when submitted to a press treatment, the samples have best mechanical properties. The pressed Hyaff.RTM.11 **non-woven** undergoes degradation when exposed to DMEM. The frying and breaking of the fibres, a decrease of the mechanical properties and a molecular weight loss have been observed. First, the ester bond of the Hyaff.RTM.11 **non-woven** is hydrolysed and the benzylic alcohol is released and the low molecular weight values indicate that a cleavage of the polymer is promoted by the components of the culture medium. After 11 days, some fragments, constituted by hyaluronic acid with a molecular weight of 23,000 Da became soluble in the medium. No oligomer was detected. .COPYRGT. 2001 Elsevier Science Ltd. All rights reserved.

L126 ANSWER 41 OF 55 TOXCENTER COPYRIGHT 2004 ACS on STN DUPLICATE 2  
ACCESSION NUMBER: 2002:58908 TOXCENTER  
COPYRIGHT: Copyright 2004 ACS  
DOCUMENT NUMBER: CA13613205509W  
TITLE: Hyaluronic acid esters, threads and biomaterials containing them, and their use in surgery  
AUTHOR(S): Bellini, Davide; Callegaro, Lanfranco  
PATENT INFORMATION: US 2002026039 A1 28 Feb 2002  
SOURCE: (2002) U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 236,958.  
CODEN: USXXCO.  
COUNTRY: ITALY  
DOCUMENT TYPE: Patent  
FILE SEGMENT: CAPLUS  
OTHER SOURCE: CAPLUS 2002:158403  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20020305  
Last Updated on STN: 20030211

AB The application discloses esters of hyaluronic acid, wherein a first part of the carboxylic functions is esterified with an araliph. alc. and a second part is esterified with at least one long-chain, straight C10-22 aliph. alc. The possible remaining non-esterified carboxylic functions, if present, are salified. The application further discloses biocompatible threads having a multifilament conformation comprising filaments formed by the hyaluronic acid esters in combination with other biocompatible polymers, such as PTFE, polyglycolic acid, polylactic acid, polycaprolactone, etc. The biocompatible threads are useful in medicine and surgery, as, e.g., sutures, scaffolds for cell culture in the form of gauzes, meshes, **non-woven** fabrics, tubes, etc. For example, a hyaluronic acid ester was prepd. by reacting 6.21 g of tetra-Bu ammonium salt of hyaluronic acid with 0.89 mL of benzyl bromide and 0.83 g of octadecyl bromide to obtain 5.1 g of **hyaluronic acid benzyl octadecyl ester**. A mixed multifilament was prepd. by extrusion of this ester in combination with a multifilament of PTFE.

L126 ANSWER 42 OF 55 TOXCENTER COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:217410 TOXCENTER  
COPYRIGHT: Copyright 2004 ACS  
DOCUMENT NUMBER: CA13710145462J  
TITLE: Physico-chemical properties and degradability of

**non-woven hyaluronan  
benzyl esters** as tissue engineering  
scaffolds

AUTHOR(S): Milella, E.; Brescia, E.; Massaro, C.; Ramires, P. A.;  
Miglietta, M. R.; Fiori, V.; Aversa, P.  
CORPORATE SOURCE: Biomaterials Unit, PASTIS-CNRSM, Brindisi, Italy.  
SOURCE: Biomaterials, (2001) Vol. 23, No. 4, pp. 1053-1063.  
CODEN: BIMADU. ISSN: 0142-9612.  
COUNTRY: ITALY  
DOCUMENT TYPE: Journal  
FILE SEGMENT: CAPLUS  
OTHER SOURCE: CAPLUS 2001:861940  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20011204  
Last Updated on STN: 20020903

AB The development of biocompatible materials which can be processed into three-dimensional scaffolds and the design of appropriate configurations in order to enable the cellular infiltration and proliferation is a major issue in the tissue engineering. The **hyaluronan** total **benzyl ester** (Hyaff11) has been found to be suitable substrate to grow a variety of cell types. Since structural, phys., chem. and biol. data can help for tailoring appropriate scaffold for tissue engineering, information on chemico-phys. properties on degradability of **hyaluronan** total **benzyl ester non-woven** has been obtained. The thermal anal., the evaluation of the surface chem. compn., the morphol., the mech. behavior and the swelling tests were carried out on these materials. The **hyaluronan** total **benzyl ester non-woven** showed a thermal stability up to 220.degree. and the surface compn. differed from that of the bulk for C-O and C-C contribution. No contaminant were detected. The **non-woven** swelled in culture medium. Moreover the mech. tests showed that when submitted to a press treatment, the samples have best mech. properties. The pressed Hyaff11 **non-woven** undergoes degrdn. when exposed to DMEM. The frying and breaking of the fibers, a decrease of the mech. properties and a mol. wt. loss have been obsd. First, the ester bond of the Hyaff11 **non-woven** is hydrolyzed and the benzylic alc. is released and the low mol. wt. values indicate that a cleavage of the polymer is promoted by the components of the culture medium. After 11 days, some fragments, constituted by hyaluronic acid with a mol. wt. of 23,000 Da became sol. in the medium. No oligomer was detected.

L126 ANSWER 43 OF 55 TOXCENTER COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:211761 TOXCENTER

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DOCUMENT NUMBER: CA13201006391U

TITLE: Biomaterials containing hyaluronic acid derivatives in the form of three-dimensional structures free from cellular components or products thereof, for the in vivo regeneration of tissue cells

AUTHOR(S): Pavesio, Alessandra; Dona', Massimo; Callegaro, Lanfranco

CORPORATE SOURCE: ASSIGNEE: Fidia Advanced Biopolymers S.r.L.

PATENT INFORMATION: WO 9961080 A1 2 Dec 1999

SOURCE: (1999) PCT Int. Appl., 37 pp.

CODEN: PIXXD2.

COUNTRY: ITALY

DOCUMENT TYPE: Patent

FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 1999:763921

LANGUAGE: English

ENTRY DATE: Entered STN: 20011116

Last Updated on STN: 20020403

AB Use of biocompatible biomaterials contg. hyaluronic acid derivs., with

three-dimensional structures enclosing **hollow** spaces created by communicating **pores** and/or **entangled** fine, **fibers** or microfibrils, free from cellular components or products thereof for the in vivo regeneration of tissue cells is disclosed. The tissue obtained by this regeneration, has the same structure, functions as the corresponding natural tissue and is well integrated in the adjacent tissue cells. **Benzyl ester of hyaluronic acid** (65% **esterification**) was implanted in bones of rats paws. After 24 days the ester induced a greater degree of bone regeneration than the total **benzyl ester** or **hyaluronic acid** in powder form.

L126 ANSWER 44 OF 55 TOXCENTER COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1994:180877 TOXCENTER  
COPYRIGHT: Copyright 2004 ACS  
DOCUMENT NUMBER: CA12120238467Z  
TITLE: Multilayer **nonwoven** tissue containing a surface layer comprising at least one hyaluronic acid ester  
AUTHOR(S): Dorigatti, Franco; Callegaro, Lanfranco  
CORPORATE SOURCE: ASSIGNEE: Fidia Advanced Biopolymers S.r.L.  
PATENT INFORMATION: WO 9417837 A1 18 Aug 1994  
SOURCE: (1994) PCT Int. Appl., 23 pp.  
CODEN: PIXXD2.  
COUNTRY: ITALY  
DOCUMENT TYPE: Patent  
FILE SEGMENT: CAPLUS  
OTHER SOURCE: CAPLUS 1994:638467  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20011116  
Last Updated on STN: 20020910

AB A multilayer **nonwoven** material, comprising a surface layer which comes into contact with the skin, such as hyaluronic acid ester, and one or more other layers which do not come into contact with the skin. This material can be employed in a wide variety of medical and sanitary applications, including surgery and as a non-adhesive covering material. A multilayer **nonwoven** tissue composed of a layer of **hyaluronic acid benzyl ester** (Hyaff 11) and a layer of **nonwoven** viscose (Jettex 2005), with 2mm thickness and water absorption of 56% was prepd.

L126 ANSWER 45 OF 55 TOXCENTER COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1993:169578 TOXCENTER  
COPYRIGHT: Copyright 2004 ACS  
DOCUMENT NUMBER: CA11916167841N  
TITLE: **Non-woven** fabric material comprising hyaluronic acid derivatives in surgery  
AUTHOR(S): Dorigatti, Franco; Callegaro, Lanfranco; Romeo, Aurelio  
CORPORATE SOURCE: ASSIGNEE: M.U.R.S.T.  
PATENT INFORMATION: WO 9311803 A1 24 Jun 1993  
SOURCE: (1993) PCT Int. Appl., 53 pp.  
CODEN: PIXXD2.  
COUNTRY: ITALY  
DOCUMENT TYPE: Patent  
FILE SEGMENT: CAPLUS  
OTHER SOURCE: CAPLUS 1993:567841  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20011116  
Last Updated on STN: 20020917

AB Biomaterials are disclosed which are comprised of biodegradable, biocompatible, and bioabsorbable **nonwoven** fabric materials. The **nonwoven** fabric materials are comprised of threads imbedded in a matrix; both matrix and threads can be comprised of hyaluronic acid esters, singly or in combination with esters of alginic acid or other

polymers. The fabric can be used for treating skin pathol., surgery, etc. Prepn. of a variety of hyaluronic acid esters is described, as is manuf. of the fabric. A **nonwoven** fabric of **hyaluronic acid benzyl ester** was impregnated with vancomycin.

L126 ANSWER 46 OF 55 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
ACCESSION NUMBER: 2003:656896 SCISEARCH  
THE GENUINE ARTICLE: 704VC  
TITLE: Gland cell cultures into 3D hyaluronan-based scaffolds  
AUTHOR: Zavan B (Reprint); Cortivo R; Abatangelo G  
CORPORATE SOURCE: Univ Padua, Dept Histol Microbiol & Med Biotechnol,  
I-35100 Padua, Italy (Reprint)  
COUNTRY OF AUTHOR: Italy  
SOURCE: JOURNAL OF MATERIALS SCIENCE-MATERIALS IN MEDICINE, (AUG  
2003) Vol. 14, No. 8, pp. 727-729.  
Publisher: KLUWER ACADEMIC PUBL, VAN GODEWIJCKSTRAAT 30,  
3311 GZ DORDRECHT, NETHERLANDS.  
ISSN: 0957-4530.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 7

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In this study we report a preliminary investigation of the feasibility of **non-woven**/sponge fabrics of a **hyaluronan** derived biomaterials (**benzyl ester** of HA (HYAFF-11(TM) FAB, Abano Terme, Italy) for the in vitro culture of rat hepatocytes and rat beta cells. Cell growth on hyaluronan derived biomaterials were tested in the presence of complete medium and in the presence of ECM (extracellular matrix) secreted by fibroblasts previously cultured into the scaffold. Hepatocytes and beta cells were extracted from rat liver/pancreas and seeded either on the HYAFF-11(TM) scaffold alone, or on HYAFF-11(TM) scaffold containing ECM. Direct assay of cell proliferation was performed with MTT test. For morphological observations samples were stained with hematoxylin and eosin. The results obtained by MTT test showed that hepatocytes cultivated in both the above described conditions were able to proliferate up to 14 days and Langerhans islet up to 21 days. After this time, cells started to undergo apoptosis. The morphological analyses showed cell aggregation in three-dimensional structures promoted by the fibers of the biomaterial.

Our results confirmed that HYAFF-11(TM) meshes represent a suitable scaffold for hepatocyte adhesion/Langerhans islet organization and proliferation. In particular, the presence of a fibroblast secreted extracellular matrix improves the biological property of the scaffold. (C) 2003 Kluwer Academic Publishers

L126 ANSWER 47 OF 55 USPATFULL on STN  
ACCESSION NUMBER: 2003:258636 USPATFULL  
TITLE: Percarboxylated polysaccharides, and a process for their preparation  
INVENTOR(S): Bellini, Davide, Montegrotto Terme, ITALY  
Crescenzi, Vittorio, Roma, ITALY  
Francescangeli, Andrea, Roma, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003181689	A1	20030925
APPLICATION INFO.:	US 2003-376369	A1	20030228 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. WO 2001-EP10062, filed on 31 Aug 2001, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	IT 2000-PD2000000020820000831	
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110	
NUMBER OF CLAIMS:	33	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	943	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	The present invention relates to percarboxylated polysaccharide selected from the group consisting of gellan, carboxymethylcellulose, pectic acid, pectin and hyaluronic acid derivatives; the process for their preparation and their use in the pharmaceutical, biomedical, surgical and healthcare fields.	
IT	111744-92-4DP, Hyaff 11, percarboxylated (prepn. of percarboxylated polysaccharides for medicinal uses)	

L126 ANSWER 48 OF 55 USPATFULL on STN  
ACCESSION NUMBER: 2003:58122 USPATFULL  
TITLE: Wound dressing  
INVENTOR(S): John Chen, Wai Yuen, Wilmslow, UNITED KINGDOM  
Moseley, Ryan, Caerau Maesteg Mid-Glamorgan, UNITED KINGDOM  
Waddington, Rachel Jane, Cardiff, UNITED KINGDOM  
Walker, Michael, Brynford, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003040690	A1	20030227
APPLICATION INFO.:	US 2002-107964	A1	20020327 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2001-7653	20010327
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ALLEN BLOOM, C/O DECHERT, PRINCETON PIKE CORPORATION CENTER, P.O. BOX 5218, PRINCETON, NJ, 08543-5218	
NUMBER OF CLAIMS:	21	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Page(s)	
LINE COUNT:	339	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	Use of a <b>polymer</b> which is swellable in aqueous media for the manufacture of a wound dressing comprising the <b>polymer</b> to reduce the concentration of superoxide radical in a wound by application of the wound dressing externally thereto. This is believed to reduce the effect of at least certain types of ROS in frustrating the healing of chronic wounds.	
IT	111744-92-4, Hyaff 11 (polysaccharides-based wound dressings)	

L126 ANSWER 49 OF 55 USPATFULL on STN  
ACCESSION NUMBER: 2003:291176 USPATFULL  
TITLE: **Three-dimensional prostheses** containing hyaluronic acid derivatives  
INVENTOR(S): Pastorello, Andrea, Abano Terme, ITALY  
Radice, Marco, Formigine, ITALY  
Callegaro, Lanfranco, Thiene, ITALY

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Brindisi, ITALY  
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6642213	B1	20031104
	WO 9965534		19991223
APPLICATION INFO.:	US 2000-719200		20001208 (9)
	WO 1999-EP4167		19990616

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1998-PD149	19980617
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	O'Sullivan, Peter	
LEGAL REPRESENTATIVE:	Hedman & Costigan, P.C.	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	752	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A **three-dimensional prosthesis** is described in the shape of a body part comprising at least one **three-dimensional** matrix having an essentially fibrous or porous structure and containing a hyaluronic acid derivative, said **prosthesis**, contains at least two of said **three-dimensional** matrixes, the first of said **three-dimensional** matrixes incorporating or being adhered to the second and possible further matrixes, said **three-dimensional** matrix(es) optionally incorporating and/or being adhered to a bidimensional perforated matrix and containing a hyaluronic acid derivative. This **prosthesis** is used for reconstruction of human or animal body part.

IT 111744-92-4, Benzyl hyaluronate  
(**three-dimensional prostheses** contg.  
hyaluronate and cells and **polymers** for reconstruction of body parts)

L126 ANSWER 50 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2003:196942 USPATFULL  
TITLE: Biological material containing bone marrow stem cells partially or completely differentiated into connective tissue cells and a hyaluronic acid ester matrix  
INVENTOR(S): Abatangelo, Giovanni, Saccolongo, ITALY  
Callegaro, Lanfranco, Thiene, ITALY  
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Brindisi, ITALY  
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6596274	B1	20030722
	WO 9718842		19970529
APPLICATION INFO.:	US 1998-41287		19980312 (9)
	WO 1996-EP5093		19961119

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1995-PD225	19951120
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Naff, David M.	
ASSISTANT EXAMINER:	Ware, Deborah K.	



LEGAL REPRESENTATIVE: Hedman & Costigan, P.C.  
NUMBER OF CLAIMS: 19  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 5 Drawing Page(s)  
LINE COUNT: 639

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A biological material comprising two components is provided containing a first component comprising alternatively (1) a culture of autologous or homologous bone marrow stem cells partially or completely differentiated into specific connective tissue cellular lines or (2) a sole extracellular matrix free from any cellular component secreted by the specific connective tissue cellular lines; and a second component containing a **three-dimensional** biocompatible and biodegradable matrix consisting of a hyaluronic acid ester having a degree of esterification comprised between 25 and 100%. The specific tissue cell lines are selected from fibroblasts, osteoblasts, myoblasts, adipocytes, chondrocytes and endothelial cells. The biological material is suitable for use as a dermal substitute in cutaneous lesions as well as repairing damaged connective tissue.

IT **111744-92-4**, Benzyl hyaluronate  
(culture of bone marrow stem cells differentiated into connective tissue cells in **three-dimensional** biocompatible and biodegradable matrix of hyaluronic acid deriv.)

L126 ANSWER 51 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2002:303586 USPATFULL  
TITLE: Biological material for the repair of connective tissue defects comprising mesenchymal stem cells and hyaluronic acid derivative

INVENTOR(S): Abatangelo, Giovanni, Via Pelosa 32, 35030 Saccolongo (Prov. of Padova), ITALY  
Callegaro, Lanfranco, Via Monte Grappa 6, 35016 Thiene (Prov. of Vicenza), ITALY  
Young, Randell G., 8418 West Grove Rd., Ellicott City, MD, United States 21043  
Murphy, Josephine Mary, 2510 Pickwick Rd., Baltimore, MD, United States 21207  
Fink, David Jordan, 303 Wendover Rd., Baltimore, MD, United States 21218  
Bruder, Scott Philip, 3698 Ashley Way, Owings Mills, MD, United States 21117  
Barry, Francis Peter, 2510 Pickwick Rd., Baltimore, MD, United States 21207  
Kadiyala, Sudhakar, 1531 Lancaster St., Baltimore, MD, United States 21231  
Caplan, Arnold I., 1300 Oakridge Dr., Cleveland Heights, OH, United States 44121  
Moskowitz, Roland, 2846 Montgomery Rd., Shaker Heights, OH, United States 44122  
Yoo, Jung U., 16301 Shaker Blvd., Shaker Heights, OH, United States 44122  
Solchaga, Luis A., 2260 Barrington Rd., University Heights, OH, United States 44118

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6482231	B1	20021119
APPLICATION INFO.:	US 2000-602033		20000623 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-39200, filed on 13 Mar 1998, now abandoned Continuation-in-part of Ser. No. US 1998-41287, filed on 12 Mar 1998 Continuation-in-part of Ser. No. WO 1996-EP5093, filed on 19 Nov 1996		

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1995-PD225	19951120
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Isabella, David J.	
LEGAL REPRESENTATIVE:	Hedman & Costigan, P.C.	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	39 Drawing Figure(s); 34 Drawing Page(s)	
LINE COUNT:	1013	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A biological material for the repair of connective tissue cells comprising:

a) a cell preparation enriched in mesenchymal stem cells,

b) **three-dimensional** extracellular matrix comprising a nyaluronic acid derivative.

The use of said biological material, optionally combined with therapeutically acceptable excipients and/or diluents and optionally in association with therapeutically effective ingredients in the repair of connective tissue cells.

IT **11744-92-4**, Benzyl hyaluronate  
(culture of bone marrow stem cells differentiated into connective tissue cells in **three-dimensional** biocompatible and biodegradable matrix of hyaluronic acid deriv.).

L126 ANSWER 52 OF 55 USPATFULL on STN  
ACCESSION NUMBER: 2001:114671 USPATFULL  
TITLE: THREADS CONTAINING HYALURONIC ACID ESTERS AND THEIR USE IN SURGERY  
INVENTOR(S): CALLEGARO, LANFRANCO, THIENE, Italy  
BELLINI, DAVIDE, MONTEGROTTO TERME, Italy

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001008937	A1	20010719
APPLICATION INFO.:	US 1999-236958	A1	19990125 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. WO 1997-EP4684, filed on 28 Aug 1997, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1996-PD207	19960829
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	JAMES V COSTIGAN, HEDMAN GIBSON & COSTIGAN, 1185 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362601	
NUMBER OF CLAIMS:	27	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Page(s)	
LINE COUNT:	654	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The application discloses esters of hyaluronic acid, wherein a first part of the carboxylic functions is esterified with an araliphatic alcohol and a second part is esterified with at least one long-chain, straight aliphatic alcohol with between 10 and 22 carbon atoms. The possible remaining non-esterified carboxylic functions, if present, are salified. The application further discloses biocompatible threads having a multifilament conformation comprising filaments formed by the aforesaid esters, and their use in the fields of medicine and surgery.

IT 203798-22-5P, Hyaluronic acid benzyl lauryl ester  
203874-06-0P, Hyaluronic acid benzyl palmityl ester  
203874-07-1P, Hyaluronic acid benzyl stearyl ester  
203874-08-2P, Hyaluronic acid benzyl arachidyl ester  
203874-09-3P, Hyaluronic acid benzyl docosanyl ester  
(manuf. and use in threads and biomaterials)

L126 ANSWER 53 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2000:134623 USPATFULL  
TITLE: Process for the coating of objects with hyaluronic acid, derivatives thereof, and semisynthetic polymers  
INVENTOR(S): Morra, Marco, Asti, Italy  
Cassinelli, Clara, Asti, Italy  
Benedetti, Luca, Vicenza, Italy  
Callegaro, Lanfranco, Vicenza, Italy  
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers, Srl, Brindisi, Italy  
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6129956		20001010
	WO 9624392		19960815
APPLICATION INFO.:	US 1997-930858		19971007 (8)
	WO 1996-EP509		19960207
			19991007 PCT 371 date
			19991007 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1995-PD30	19950207
	IT 1995-PD243	19951220
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Cameron, Erma	
LEGAL REPRESENTATIVE:	Birch, Stewart, Kolasch & Birch, LLP	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	14 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	1246	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Processes are provided for coating the surfaces of objects with hyaluronic acid, its derivatives or other natural or semisynthetic polymers, for applications in the fields of surgery, health care and diagnostics. The processes make it possible to bind such polymers in a stable manner to the surfaces of objects made of a wide range of materials. Surfaces treated according to the processes are characterized by a high degree of wettability, and are able to inhibit the adhesion of cells or bacteria present in the biological fluids.

IT 111744-92-4, Benzyl hyaluronate  
(coating of objects with hyaluronic acid, derivs., and semisynthetic polymers)

L126 ANSWER 54 OF 55 USPATFULL on STN

ACCESSION NUMBER: 1999:96274 USPATFULL  
TITLE: Hyaluronan based biodegradable scaffolds for tissue repair  
INVENTOR(S): Valentini, Robert F., Cranston, RI, United States  
Kim, Hyun D., Providence, RI, United States  
PATENT ASSIGNEE(S): Brown University, Providence, RI, United States (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION: US 5939323 19990817  
 APPLICATION INFO.: US 1997-864709 19970528 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-18492P	19960528 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Witz, Jean C.	
ASSISTANT EXAMINER:	Hanley, Susan	
LEGAL REPRESENTATIVE:	Wolf, Greenfield & Sacks, P.C.	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	848	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A hyaluronic acid derivitized scaffold and method of forming are disclosed. The scaffolds are useful for various medical purposes such as tissue repair, tissue reconstruction and wound healing. In order to enhance these processes the scaffolds may be engineered to incorporate biologically active molecules such as BMP.

IT 111744-92-4, Hyaluronic acid benzyl ester  
 (hyaluronan-based biodegradable scaffolds for tissue repair)

L126 ANSWER 55 OF 55 USPATFULL on STN

ACCESSION NUMBER: 97:73299 USPATFULL

TITLE: Multilayer **nonwoven** tissue containing a surface layer comprising at least one hyaluronic acid ester

INVENTOR(S): Dorigatti, Franco, Trento, Italy  
 Callegaro, Lanfranco, Padua, Italy

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Brindisi, Italy  
 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5658582		19970819
	WO 9417837		19940818
APPLICATION INFO.:	US 1995-505325		19951010 (8)
	WO 1994-EP397		19940211
			19951010 PCT 371 date
			19951010 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	IT 1993-PD24	19930212
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Page, Thurman K.	
ASSISTANT EXAMINER:	Shelborne, Kathryne E.	
LEGAL REPRESENTATIVE:	Birch, Stewart, Kolasch & Birch, LLP	
NUMBER OF CLAIMS:	26	
EXEMPLARY CLAIM:	1	
LINE COUNT:	485	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided is a multilayered of **nonwoven** material comprising a surface layer which comes into contact with the skin, and one or more other layers which do not come into contact with the skin, wherein said surface layer which comes into contact with the skin is a member selected from the group consisting of a surface layer comprising at least one hyaluronic acid ester, a surface layer comprising a mixture of said at least one hyaluronic acid ester and at least one natural

**polymer**, semisynthetic **polymer**, or synthetic **polymer**, and a surface layer comprising a natural, synthetic, or semisynthetic biocompatible perforated membrane compatible with cell growth on its surface. This material can be employed in a wide variety of medical and sanitary applications, including surgery and as a non-adhesive covering material.

IT **111744-92-4**, Hyaluronic acid benzyl ester  
(multilayer **nonwoven** tissue contg.)

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